

Almost the Last Word on the Club of Rome

It is now just over a year since Professor Dennis Meadows and his colleagues at the Massachusetts Institute of Technology published their tract *The Limits to Growth* under the auspices of the Club of Rome, and their argument has been a powerful stimulant of all kinds of public discussion. Because the complicated apparatus of mathematical equations which form the basis of Meadows's model has lent an air of mathematical precision to this work, the conclusions of *The Limits to Growth* have frequently been regarded as a proof of more qualitative gloomy predictions of what the future would be like. And because many politicians appear to welcome the great excitement about the natural environment there has been in recent years as an opportunity for effecting changes which might otherwise be politically impractical, *The Limits to Growth* has had an important influence on the attitudes of several governments—in Italy, for example, the general thesis that there are imminent dangers of collapse is understandably welcomed as a kind of explanation of the difficulties of regulating the economy of Italy.

Yet the tentative criticism which has been possible of *The Limits to Growth*, hampered as it has been by the lack of sufficient information about the assumptions on which the model has been based, has by now, in technical circles, led to the conclusion that the best thing to be said of the complicated model at MIT is that it is one of the most ambitious exercises in computer modelling so far undertaken which would have been of greater value if only greater care had been taken to make the assumptions explicit.

The irrelevance of *The Limits to Growth* to practical problems has now been finally underlined by the publication of a series of studies by the Science Policy Research Unit at the University of Sussex (*Futures*, 5, 1; 1973). The argument of Professor Christopher Freeman and his colleagues is all the more convincing because of its moderation. For example, Freeman says that he and his colleagues at Sussex are "in complete agreement" with the "MIT authors and their sponsors" about the urgency of many of the social problems with which *The Limits to Growth* is concerned. He also says that there is no quarrel about the desirability of mathematical models in the social sciences. Freeman is even generous saying that the construction of Meadows's computer model is "courageous and pioneering"—others may fairly say that it is brash and even foolhardy. The nub of the criticism from Sussex is that the assumptions used in constructing the Meadows model do not correspond accurately enough to the real world for the computer projections to be regarded as reliable guides to action in future. The Sussex team goes on to make the sensitive point that in circumstances in which the overriding need is to use the techniques of computer modelling as a method of understanding the relationship between different sociological variables, itself a formidable task, there is bound to be an element of subjectivity in ambitious schemes of computer modelling, and that it might be better to acknowledge that

exercises like that of Meadows and his colleagues should openly be regarded as components of a political debate.

The Sussex criticism is based on the published volume *The Limits to Growth* and on an early draft of the technical report which was originally said to be due for publication in 1972. By all accounts, publication of this crucial document, in its final form, will now be delayed at least until the summer of this year. The Sussex criticism is accompanied by a rebuttal from Professor Meadows and his colleagues which raises important issues about the professional ethics of scientific discussion in this field. Thus Meadows says "inexplicably, the Sussex group has chosen to release its criticism before the last technical document becomes available to the scientific community" and elsewhere says, in a footnote, that advance copies of the technical report are available in photocopied form already. What Meadows implies is that scientific criticism of *The Limits to Growth* should have been held over until the much postponed technical description of the assumptions on which the computer model is based had been completed. What he overlooks is that one of the most damaging criticisms of his exercise in computer modelling is that *The Limits to Growth* itself should not have been published without a full description of its assumptions. Undergraduates instructed in the techniques of computer modelling are—or should be—told quite firmly that a model is of no value to others unless its assumptions are made explicit and are open to technical discussion. What Meadows seems to be asking for is the best of both worlds—he wants *The Limits to Growth*, with its stark and astonishing projections of the future, to inform the political decisions of governments but that technical criticism from his professional colleagues should be held up until he gives the signal. The truth is, however, that *The Limits to Growth* itself contains enough errors and inconsistencies to sustain the kinds of criticism which the Sussex group and others have advanced. If it should be that the final version of the accompanying technical report turns out to make the absurdities of *The Limits to Growth* less obvious, it will be an important public question to know whether that document should be regarded as the guide to action which the Club of Rome hoped it would be. It should perhaps be added that advance copies of the technical report are not nearly as freely available as Meadows says—he has, for example, declined to supply one to *Nature* on the grounds that "you will only use it against us". It is hoped that the muddle—to say the best of it—created by this slapdash method of publishing a scientific thesis will be a warning to others who may follow with computer projections of the future.

In detail, the criticisms which the Sussex group has to make echo the previous criticisms which have been made of *The Limits to Growth*. First of all, the group emphasizes that the validity of any computer calculation depends entirely on the quality of the data and the assumptions which are fed into it, and warns against the dangers



of "computer fetishism". Somewhat generously, the Sussex group defends Meadows against the implications of the charge "garbage in, garbage out", but goes on to assert that although the Meadows model is not strictly Malthusian, it is fair to level at the MIT work the jibe "Malthus in, Malthus out". What this implies is that the parts of the MIT model dealing with population make no allowance for the way in which population growth is determined—as the demographic history of the past century shows clearly enough—by changes in family habits just as much as by physical considerations. The Sussex group also points to the now well-known weaknesses of *The Limits to Growth* model and its assumptions of how mortality, for example, is related to worldwide levels of pollution, an issue on which there is no scientific evidence on which to base assumptions of any kind. The criticism continues with an account of how the assumptions in the model of the likely exhaustion of natural resources are over-simple and over-rigid. The plain truth is that anyone who assumes that there is a literally finite supply of natural resources—250 years supply of everything at the present rate of consumption in the original Meadows model—and who neglects such things as the influence of the price mechanism on the rate of consumption and the likelihood that new discoveries will be made in the future as in the past will inevitably conclude that there must at some stage in the future be a catastrophic collapse of the industrial economy. Yet in the long run, the most likely happening is that industry will be compelled by the increasing scarcity of some of the materials now inherently a part of industrial life to switch to others which are intrinsically much more plentiful. This is a splendid example of how the supposedly objective Meadows model turns out to contain a built-in bias in favour of collapse in the not too distant future.

The Sussex group rehearses other now familiar difficulties with the Meadows model, but does so moderately and with the advantage of knowing what the early draft of the famous technical report contains. There are arithmetical inconsistencies as well as economic anachronisms built into the parts of the calculation dealing with capital investment. The relationship between industrial activity and the generation of pollution assumed in the model is over-simple and misleading. The computer loops dealing with agricultural productivity make too little allowance for beneficial change. In all the circumstances, it would have been more prudent if Meadows, in his reply, had been more willing to acknowledge the cogency of these criticisms. Instead, he blusters, complaining that "the Sussex authors have not put forward an alternate (*sic*) theory of growth to support their views", as if it were incumbent on critics always to follow the precedents of those they criticize. He goes on to complain, unfairly, that the work of the Sussex group implies that "present short-term reductionalist predictive models are appropriate for addressing the causes and consequences of population and material growth"—the point is that the papers from Sussex acknowledge that the problems which worry Professor Meadows and other people are legitimate concerns but raise the question whether they can properly be handled by computer models in the present state of uncertainty. Meadows seeks to distinguish between "the numerical properties of our preliminary world models" and the "basic dynamic attributes" of the world system described in *The Limits to Growth*, arguing that exponen-

tial growth in a physically limited world leads to inherent instability, and that this aspect of the problem demands urgent study "whether or not the precise assumptions of our particular computer model are ultimately accepted". In reality, however, what the Sussex group, like previous critics, has done is to point out that the mechanisms of exponential growth and the assumptions of rigid physical limits which characterize *The Limits to Growth* are themselves untenable: the argument is only partly about numbers and is more cogently concerned with the character of the assumptions made. Against this background it is hard, with the best will in the world, to accept seriously Meadows's own list of "the errors" which the Sussex group has allegedly made. Indeed, some of the details of the Sussex work which Meadows describes as erroneous deserve some quite different description altogether. It is, for example, absurd of him to complain that it is an error for the Sussex group to argue that not enough is at present known of the ultimate availability of natural resources and then to go on to say that the estimates in *The Limits to Growth* are too conservative. Is Meadows really wishing to imply that in circumstances in which certainty is unattainable, it is legitimate for those who build computer models to make whatever assumptions they choose, even when these are known to be too limited?

The essence of the Sussex criticism is that the Meadows model is too inaccurate a representation of the real world to be a reliable projection of the future, but the issue of principle which divides the two groups is their attitude towards technical progress. It has been said, of *The Limits to Growth*, that many of the gloomy projections stem directly from the assumption that present gloomy trends—the pace of population growth, for example—will continue as they are until checked by physical shortages, but that recent optimistic trends, such as the steady improvement of agricultural productivity and the development of new techniques for the exploration for and the exploitation of new mineral resources, will come to a halt. It is true that nobody can predict just what technical skills will be accessible to the human race decades from now, but surely it is quite absurd, after the experience of the past century, to suggest that there will be no improvement of the techniques by which people at present survive on the surface of the Earth. To say this is in no sense to imply that scientific research and technical development contain in themselves the secret of survival, but there is the strongest possible reason for expecting that technology will continue in some shape or form. Indeed one of the morals that might have been drawn from *The Limits to Growth* is that there is an urgent need for scientific research and technical development in some of the areas such as energy supply in which Meadows and his colleagues do not have a monopoly of concern. It is fashionable among some environmentalists to complain of those who would allow for the likelihood that survival skills will continue to become more sophisticated as "technological optimists". What that canard implicitly denies is that the survival of the human race so far, in the past five hundred thousand years or more, has depended on a continual enhancement of skill and that, even if it were now possible to halt some of the tendencies such as population growth which cause anxiety, survival would require a continuing search for better techniques. Computer modelling itself is such a skill. What this argument has shown is that there is still a long way to go.

Five Years More

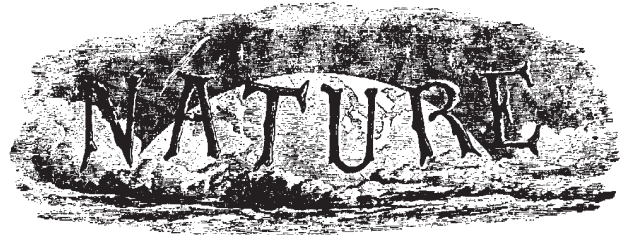
THE British government is wise to have acknowledged that it cannot hope to work out a long-term strategy for broadcasting in Britain by the time the franchise of the BBC and the constitution of the Independent Broadcasting Authority are due to be revised in 1976, but it is less certain whether a postponement of the decision until 1981 is strictly necessary. Everybody will agree that it would be wrong to rush a decision on long-term strategy without first carrying out the technical studies and the consultations on which a sound policy might be based, but a postponement of five years is almost the same as a decision not to think about the broader issues in the lifetime of the present Parliament or even, possibly, during that of the next. To be sure, the government has said that it will push ahead with a decision about a fourth television channel and that it feels free to think again about the method of financing the BBC's operations, at present dependent on licence fees collected from the public. But there is the strongest possible case for asking that a quick start should be made on several issues likely to determine the pattern of broadcasting in the 1980s.

One important issue, for example, is the extent to which the BBC should continue in its present form as an autonomous organization responsible both for the production of programmes and for the transmission of electromagnetic waves. The corporation's competence and reputation in both fields is outstanding but it would be an economy and probably a qualitative benefit as well if the engineering side of the corporation's function were amalgamated with that of the Independent Broadcasting Authority. It is, of course, essential that in any reorganization of the BBC, the editorial independence of the programme-making function should be guaranteed and it is even proper to ask whether this might not in future be more safely assured if the corporation's trustees, the Board of Governors, were provided with an annual grant and not the necessarily uncertain and static revenue from licence fees.

A second group of questions is technical. Largely because Britain is geographically crowded, the number of television channels available at the UHF band is limited, with the result that British television is unlikely ever to consist of more than four channels so long as old-fashioned broadcasting is the principal method of transmitting signals. This is why it is inevitable that there should be a rapid growth of cable television in the decades ahead. One of the questions to be decided is who should own and operate a cable television network, and how arrangements should be made for supplying it with programmes. Technically, there is the strongest possible case for an integrated network of cables through which a variety of programmes could be supplied. The ideal, no doubt, is that the network should be publicly owned and that it should be possible for its operators to make charges on those who use it in much the same way as telephone subscribers now pay different charges for different kinds of telephone calls. But the government should not let its hankering after control delay the introduction of an essential service like this when commercial companies are only too ready to provide the capital. The first need, in any case, is for a further technical examination of the problem but the second is for an examination of the problems in providing

a cable television network of programmes—one of the virtues of the system is that it should make possible local community broadcasting, another is that it should allow people to have television programmes from other countries, no doubt at a different price. It will be a scandal if this is much delayed.

100 Years Ago



THE CHALLENGER EXPEDITION

H. M.S. *Challenger* cast off from the jetty at Portsmouth at 11.30 A.M. on December 21, with a low barometer. A strong south-westerly breeze was blowing, and the drum up; so that, especially in a season like the present, the prospect was not promising for the first few weeks of her voyage round the world.

The result justified the drum, and for a week we were knocking about the mouth of the Channel, and the Bay of Biscay, making slow progress southwards. It was perhaps as well to get a good shaking at first. It showed at once where there was a screw loose, and gave a chance to tighten it up. A sharp cyclone which caught the ship on her way from Sheerness to Portsmouth had already tested pretty fully the stowing of the apparatus, and although the *Challenger* rolls considerably when she is put to it (over 35°), not a single instrument shifted, and not a glass was broken, either in the zoological work-room, or in the chemical laboratory. Just before we got to Lisbon the weather improved a little, and we got some soundings and took one or two trial hauls with the dredge.

After leaving Lisbon on January 12 the wind was again fresh, but between Lisbon and Gibraltar we made some important experiments, and found, among other things, that we could work easily and successfully with the common trawl down to 600 fathoms. I am now writing about 100 miles north of Madeira, and since leaving Gibraltar the weather, though at first breezy, has been on the whole fine. We have taken several successful navigative sounds at great depths, and we have trawled successfully at 2,125 fathoms, and recovered many interesting animal forms, several of them new to science, and others of extreme rarity and beauty. Still we must regard our work up to the present time as only tentative. The weather has been against us. It is altogether a new experiment to dredge from so large a ship, and it seems to present some special difficulties, or at all events to require some management. The weight of the ship is so great that there can be no "give and take" between it and the dredge, such as we have in the case of a smaller vessel. If there is any way on, the impulse to the dredge is irresistible, and seems to tend to jerk it off the ground. This difficulty can no doubt be met, but the only way of meeting it appears to be by using a length of rope greatly in excess of the depth—and having weights. A single dredging operation may thus occupy a great length of time, but in compensation we have the greater size and efficiency of this dredge. The few trials which we have already made have been all in the direction of improvement, and I have little doubt that under Captain Nares' skilful management what little difficulty is still felt will shortly disappear. • • • • •

WYVILLE THOMSON

From *Nature*, 7, 385, March 20, 1873.

OLD WORLD

Launchers for Europe?

THE question of whether United States rockets will be used to launch European communications satellites was carried right into the American camp last week. Professor Maurice Levy, chairman of the council of the European Space Research Organization, took the opportunity of an address to the American Astronautical Society in Washington to demand a guarantee from the Americans that their launchers will be available for European communications satellites as well as for scientific and other applications satellites. Otherwise, he said, Europe will have to envisage continuing her own launching activities.

The United States has already given general assurances that any country's scientific and applications satellites will be launched provided that they are for peaceful purposes and that the obligations of the United States under international arrangements and agreements, such as Intelsat, are honoured. But the offer of launchers for communication satellites is hedged about with conditions that make it anything but an open assurance.

So far, all Europe's scientific satellites have been launched by the United States. But when Europe's first communications satellite becomes due for launch in 1979 or 1980, commercial considerations will come to the fore for the first time. What Europe wants is a plain statement from the United States that all its satellites will be launched, regardless of commercial interests.

"The Europeans," Professor Levy said, "will endeavour to avoid duplication and waste in the space field. . . . If Europe can obtain a real guarantee that American launchers will be supplied for all European satellites developed for peaceful purposes, then the community of European countries may consider giving up their own launcher programmes. . . . Only real guarantees on the granting of licences for the construction of launchers, and more generally on the availability of American launchers, could lead Europe to reconsider her position".

The problem, for ESRO, is one of some urgency. Three applications satellites were approved by the organization's council in 1971, and the launch date for the first of these is only three years away. The chances of the European Launcher Development Organization having the French-designed L3S ready for operation by then must, on past showings, be remote. The rocket is still largely on the drawing board even though it uses some existing com-

ponents, and ELDO is about to go through a time-consuming reorganization as it becomes part of the proposed European Space Agency which is to come into existence on January 1 next year.

With two of ESRO's three applications satellites there should be no problem. AEROSAT, part of an international air traffic control programme, is in any case a shared programme with the Americans, so a launcher for that in 1976 is no problem. Similarly ESRO's meteorological satellite, part of the World Weather Watch programme and also due for launch in 1976, presents no commercial threat to the United States.

But ESRO's European Communications Satellite (ECS), a test version of which is to be flown in 1976 and full versions of which are planned for 1979 or 1980, is another matter. Designed for intra-European communication the satellite will handle telephone, telegram,

telex and television channels and must be considered viable.

Professor Levy emphasised in his speech recently that one of the most important objectives of Europe's space programme for the 1980s is to meet user requirements. This involved, he predicted, not only communications satellites but also relay satellites served by numerous small terminals designed to meet the specific requirements of users such as newspapers and banks.

But before ESRO has to have launchers for its communications satellites, the French and Germans need one to launch their communication systems *Symphonie I* and *II*. At present these are to be launched on Europa II, but the programme may well be scrapped before their launch date (see *Nature*, **241**, 359; 1973), in which case an American (or Russian) launcher will be the only way to fly the satellite, and the indications are that the Americans will launch it.

CONTRACT RESEARCH

Fulmer-Yarsley Merger

THE Fulmer Research Institute, owned by the Institute of Physics, is to merge with Yarsley Research Laboratories (YRL) to form a company with a turnover of £750,000 a year. Fulmer confidently expects this figure to rise to £1 million a year in 1975.

Fulmer and Yarsley are no strangers to each other, for each company has in the past done sub-contracting work for the other. But after May 1, 1973, the links will be much closer and will allow the new company to offer customers a wide range of expertise. In the past, Fulmer has been noted for its work on surface coating and alloy development among other things whereas YRL has been strong on polymers and plastics.

YRL at present operates at Chessington, Surrey, where there is little room for expansion and, through its subsidiary Yarsley Technical Services (YTL) at Ashstead, Surrey. The plan is that the activities at Ashstead will continue as before, although the shares in YTL will be held by Fulmer, but that work at Chessington will be transferred to the new Yarsley laboratories at the Fulmer site in Stoke Poges by the end of September.

The new combined concern will employ 200 staff of whom 85 are professionally qualified. In 1971 Fulmer had a turnover of £467,000 and made a profit of £15,000 after paying £12,500 to

Turnover of British Independent Contract Research Organizations (1970)

	£ thousand
Huntingdon Research Centre	2,000
International Research and Development	1,100
Robertson Research International	740
Ricardo and Co.	740
Fulmer + Yarsley	590
Inveresk Research International	250

the Institute of Physics. The profit for 1970 was much higher—£25,500—but in that year the Institute of Physics received only £9,100 (see *Nature*, **232**, 4; 1971). Also Fulmer spent £12,000, a particularly large amount, on taking out patents in 1971. YRL, on the other hand, had a turnover of £220,000 in 1971-2 and made a modest profit of £4,000.

How will the new Fulmer Research Institute compare with other contract research organizations in Britain? The Table shows the situation in 1970. Evidently Fulmer will be within striking distance of the four largest companies when the merger is complete. Overall, contract research in Britain is now worth about £12 million a year, which includes more than £3 million from contract research activities at Harwell. This is still much less than the amount spent in the United States on contract research; there the total market is more than £250 million a year and the largest companies, the Battelle Institute and Stanford Research, each have an annual turnover of about £50 million.

URANIUM ENRICHMENT

European Plant Planned

PRESSURE is growing for a European uranium enrichment plant. A report by the Parliamentary Committee on Energy, Research and Atomic Problems, which is to be presented to the European Parliament on Saturday this week, urges the community to establish a joint undertaking to study the problem of uranium enrichment in order to provide, by June 30, 1974, for a decision to be taken on which system should be built commercially.

The committee's report backs up almost to the last detail the recommendations that the European Commission has been making for some time. Two years ago the commission pointed out that by 1980 there would be a marked shortage of uranium enrichment capacity in the world. By 1980 Western Europe will be generating 70,000 MW of electricity by nuclear power; by 1985 output will have risen to 160,000 MW, according to the commission.

Enriched uranium is currently supplied by the United States Atomic Energy Commission, but its capacity will be only 26 million separative work units by 1980, and Europe's requirements alone will be 10 million SWUs in 1980 rising to 19 million units by 1985. As a result, the commission concludes that nuclear power stations ordered after 1974 cannot be sure of supplies of enriched uranium unless Europe builds its own plant.

The commission sent a draft resolution to the council of ministers last year urging it to establish a joint undertaking to study the problem. It is this recommendation that the parliamentary committee has now backed.

But the parliamentary committee emphasizes in its report that unless a political decision on a community energy policy is taken, no decision on a uranium enrichment plant can be made. Ministers are meeting to discuss, and hopefully devise, a common energy policy in May.

The committee's other chief recommendation is that, at first sight, there is no reason why more than one uranium enrichment method should not be developed by the community. Part of the problem is that there are three methods available; the question is which to choose.

Gaseous diffusion is the traditional method and is used in the United States. Nozzle separation, which is being studied in West Germany, is still in its infancy and is unlikely to be in the running for some years yet unless an enormous amount of effort is put into it. The gas centrifuge is the real alternative to gaseous diffusion. Britain has worked on the gas centrifuge for

some years now and in 1971 a joint company was formed between Britain, Holland and West Germany to study ultracentrifuge separation.

Its protagonists claim that the centrifuge will ultimately prove far more economic than gaseous diffusion. Dr Jack Parry, technical director of URENCO, the marketing part of the tripartite centrifuge project, told a conference in Tokyo last week that from an investment point of view the centrifuge now looks viable. Backers need to be sure that the capital cost of plant can be predicted accurately before they agree to invest in it. "We have no hesitation in believing this to be the case," Dr Parry said.

An additional spur to the European programme is the proposal by the United States to raise its prices for enriched uranium by more than a third. Such an increase could go some way to making the centrifuge more economic more quickly.

SCIENTIFIC JOURNALS

ZhETF Centenary

from our Soviet Correspondent

THE Russian *Journal of Experimental and Theoretical Physics* (*Zhurnal Eksperimental'noi i Teoreticheskoi Fiziki—ZhETF*) is this year celebrating the centenary of its publication. This journal, the oldest Russian periodical devoted to the physical sciences, started life as the official organ of the Russian Physical Society which was founded in March 1872. The first issue of the journal appeared early the following year.

In 1878, the Russian Physical Society amalgamated with the Chemical Society, and the joint publication of the combined body became the *Journal of the Russian Physico-Chemical Society* (*Zhurnal Russkogo Fiziko-Khimicheskogo obshchestva—ZhRFSKhO*). The physics section of this journal, however, retained its separate pagination and its own editor and was virtually still an independent journal. In 1907 it once again resumed separate publication.

During its existence as the physics section of *ZhRFSKhO*, its contributors included such eminent names as D. I. Mendeleev, P. S. Erenfest, V. K. Lebedinskii, and A. F. Ioffe. Up to 1917 its size remained small, averaging only thirty printed pages a volume.

The *ZhRFSKhO* survived under its old title until 1930, when, as part of a general reorganization of scientific societies and institutes, it was transformed into its present form as the *Zhurnal Eksperimental'noi i Teoreticheskoi Fiziki*. Since then its editors have been A. I. Ioffe and L. I. Mendel'shtam (1931–39), S. I. Vavilov (1939–52), N. N. Andreev (1952–56) and P. L. Kapitsa (1956–).

ENVIRONMENT

Whiskey in the Jar

THERE is little fear that man will exhaust the mineral resources of the Earth, according to Professor D. D. Hawkes of the University of Aston. Delivering his inaugural lecture as professor of geological sciences, Dr Hawkes maintained not only that the 17 million million tons of material in the outer ten miles of the Earth's crust contain enough metal to meet all man's needs provided he can extract it, but also that ores are still being formed.

Manganese nodules may be accumulating some minerals faster than man currently uses them, hot brines containing abnormal quantities of Mn, Zn, Cu, Pb, and Ag are forming beneath the Red Sea, and volcanoes can and do produce economic deposits—for example the 160 million tons of ore deposit (with an average content of 35 per cent) found in the Matsuo crater.

Professor Hawkes also took issue with estimates of current reserves. Based as they are on the limited data available which list only known deposits of ore and which assume no progress in mining or prospecting technology, they are "always unreliable and invariably on the pessimistic side".

The ocean floor may well contain large quantities of ore, and a "great untapped mineral potential" lies beneath the continental crust. This crust is more than 25 miles thick in places but radically new methods of mining could enable man to conquer the "depth barrier".

Professor Hawkes went on to urge that a wide-ranging survey of Britain's mineral deposits should be launched, complete with exploratory drillings. Further, parliament should pass an act declaring all minerals the property of the state, for private ownership of mineral rights in Britain causes serious delays in the development of Britain's mineral resources.

Professor Hawkes also defended the findings of Lord Zuckerman's commission on mining and the environment which was sponsored by Rio Tinto Zinc and six other large mining companies.

Mineral prospecting in National Parks also received Professor Hawkes's approbation. Prospecting and exploratory drilling, he argued, causes little damage to the environment. After full-scale mining "the environment—admittedly in a changed form—is still there", and the change need not be a great one. A different emphasis in our attitude to the environment is needed, Professor Hawkes said. "If a copper deposit is discovered in North Wales, should we not be saying—'how can we mine it with least interference to the environment?'". Not, as at present, 'North Wales is beautiful; we cannot have a mine there'."

NEW WORLD

Human Experimentation and Medical Ethics

by our Washington Correspondent

FOR the past 40 years, a number of poor uneducated black men in Alabama have been taking part in a medical experiment without their knowledge or consent. They were all found to have syphilis in 1932, but treatment has been withheld from them—even after penicillin became available—because the investigators wanted to determine the clinical effects of untreated syphilis. The experiment, known as the Tuskegee Study after the Alabama town in which it took place, was brought to light last year by a reporter working for the Associated Press, and it has become perhaps the most visible scandal involving medical research in the United States.

When the Tuskegee study first hit the headlines, government officials pointed out that although the study was carried out by the Public Health Service, they were unaware of it. They promised to provide free health care to the survivors (a promise which has yet to be kept) and pointed out that the study was initiated 40 years ago, when medical practice and social conditions were very different—guidelines and controls on medical research are now sufficient to prevent such abuses taking place, it was suggested. But several witnesses who testified before the Senate Health subcommittee during hearings on human experimentation last week were much less sanguine.

The hearings brought to light a number of abuses of medical practice which Senator Edward Kennedy, the chairman of the subcommittee, described as "outrageous". The committee was told, for example, of a study carried out last year in San Antonio, Texas, in which a number of Mexican-American women who went to a family-planning clinic were given placebos instead of oral contraceptives as part of a study to determine whether the side effects of the pill are physiological or psychological. Although told to continue practising whatever form of birth control they usually used, at least ten of the women quickly became pregnant.

In another case, an experimental method of inducing abortion was carried out on 15 women in Philadelphia in May last year, as a result of which one eighteen-year-old woman had to have a complete hysterectomy and eight others had complications. According to Dr Sidney Wolfe, a doctor associated with an organization called the Health Research Group which is linked with Ralph Nader, the method, known as the super-coil, had previously been condemned as

scientifically unsound and the women on whom it was used were not adequately informed of the risks involved. In a previous set of hearings, (see *Nature*, 242, 7; 1973), Kennedy's subcommittee had also brought to light incidences of routine prescribing of drugs for uses not approved by the Food and Drug Administration.

Fortunately, such cases of seemingly obvious abuse of medical ethics in research involving human subjects are rare, but several witnesses suggested last week that they simply represent the tip of an iceberg of questionable research practices and studies which have dubious scientific merit. Such a situation led many to recommend that controls over human experimentation should be strengthened.

In 1971, the Department of Health, Education and Welfare (HEW) published a set of guidelines for all the research involving humans which it supports. The guidelines reflect the objectives spelled out in the Nuremberg

Code promulgated by the judges at the trial of Nazi war criminals. In short, they specify that three chief criteria must be fulfilled in any experiments on human subjects. First, the risks to the subject must be outweighed by the potential benefit to him or by the importance of the knowledge to be gained. Second, the subject must be fully informed of the possible risks, and he should give his consent without any coercion. And third, committees should be set up in institutions in which research on humans takes place to review the necessity for the research and to ensure that it is carried out ethically.

In theory, those applying for research grants from agencies in HEW must comply with the guidelines and, similarly, drug companies which apply to the Food and Drug Administration for permits to conduct drug trials should also comply with the guidelines. But, according to Dr Jay Katz of the Yale University School of Law and author of a book on *Experimentation with*

HEALTH RESEARCH

White House Lunacy

by our Washington Correspondent

THE Nixon Administration's plans for cutting back in some areas of biomedical research and for phasing out the NIH training grants and fellowships were described last week as "lunacy" by Professor James D. Watson, director of the Cold Spring Harbor Laboratory and professor of molecular biology at Harvard University. Testifying at the Senate Health Committee hearings on human experimentation, Watson also castigated the Administration for concentrating on research likely to have a quick payoff at the expense of more basic research. "This way of proceeding," he said, "represents a puerile understanding of both how good science is done and how its discoveries have been directed toward human application."

The object of Dr Watson's remarks was the Administration's budget for 1974, which proposes cutbacks in funding for every institute in the National Institutes of Health except the National Cancer Institute and the National Heart and Lung Institute, and the phasing out of all grants and fellowships administered by the NIH for training new researchers.

But Watson was not alone in his concern, for no less an authority than Dr Michael DeBakey, the renowned Houston heart surgeon, and Dr Lewis

Thomas, dean of the Yale School of Medicine, told the subcommittee of their misgivings. And Senator Edward M. Kennedy, the subcommittee's chairman, did not miss the opportunity to criticize the Nixon Administration, promising that he would do what he can to restore some of the money.

But it is not simply the cutbacks that concern Dr Watson, for he also expressed strong reservations last week about the trend towards more targeted research and in particular the use of contracts instead of grants for scientific programmes. He pointed out that "almost every important new discovery comes from someone under thirty-five and who at the moment of his breakthrough is essentially unknown to the outside world", and such people are thus unlikely to receive contracts "from a government that looks with distaste on the unpredictable".

As for the phasing out of training grants and fellowships, Watson predicted that "not only will all the money be tightly held by middle-aged entrepreneurs, but the science itself will have for the most part to be done by an age-group not noted for working into the night". Asked by Kennedy where the Administration gets its advice for the plans for biomedical research, Watson said that none of his colleagues supports the plans, and that the National Cancer Board, the chief advisory body for cancer research of which Watson is a member, "is not listened to".

Human Beings, although the guidelines "have provided some significant controls over research practices . . . they are inadequate and . . . the problems remain unsolved".

Those sentiments were echoed by several other witnesses at the hearings, and in particular by Dr Bernard Barber, chairman of the Department of Sociology at Columbia, who outlined the results of a survey of some 350 medical researchers engaged in 424 different studies involving human subjects. Dr Barber found that information supplied by the researchers themselves indicated that eighteen per cent of the studies involved more risk than benefit for the subjects, and even after the possible long-term benefits to society were included in the analysis, 8 per cent of the experiments involved more risk than benefit. Moreover, 9 per cent of the respondents in the survey volunteered the information that their research had not been subjected to peer review.

What steps should be taken to tighten control over human experimentation? Both Dr Barber and Dr Katz suggested that Congress should pass legislation setting up a board with authority to regulate at least federally funded research involving human subjects. Last year, the Senate passed a resolution sponsored by Senator Walter Mondale calling for a commission to study and make recommendations in the general area of medical ethics, but the proposal died in the committee rooms of the House of Representatives. Katz and Barber believe, however, that Congress should go one step further and set up a regulatory, rather than simply a study, organization.

The idea would be for the board to consist of people drawn from several disciplines and to include lay members. It would formulate detailed policies on such issues as the selection of subjects, informed consent and the application of risk-benefit criteria, and it would firmly guide the work of peer review committees in research institutions. Katz also suggested that the board should be independent of HEW so that it could have control over research sponsored by agencies such as Defense.

Other suggestions aired at the hearings included an immediate moratorium on research involving prisoners. Such experimentation is more extensive in the United States than in any other Western country, and it involves special issues such as the difficulty of obtaining genuinely free informed consent from a person who effectively has little freedom of choice. A number of serious abuses of medical ethics in prison research were detailed at the hearings last week (see box). It was also suggested that scientific journals should refuse to publish research results derived from studies involving unethical practices.

PRISON RESEARCH

Ethics Behind Bars

by our Washington Correspondent

IN April 1971 another priceless piece of information was added to the scientific literature with the publication of a paper describing the effects of vitamin deficiency in prisoners in Iowa State Penitentiary. To obtain the information, five prisoners were fed a diet deficient in vitamin C for up to three months, and the onset of scurvy was carefully monitored. The clinical signs included swollen and bleeding gums, loss of hair, haemorrhages in the skin and eyes, pain in the joints, loss of dental fillings and depression.

That is just one particularly outrageous example of research conducted on prisoners, described last week during hearings on human experimentation held by Senator Kennedy's Senate Health subcommittee — but the hearings also brought out the fact that the majority of preliminary drug testing in man in the United States is done behind prison walls.

According to Dr C. Joseph Stetler, president of the Pharmaceutical Manufacturers Association, about 70 per cent of Phase I drug tests — the preliminary safety studies which follow immediately after animal testing — are carried out on prisoners.

Dr Stetler defended the use of prisoners for drug testing on the grounds that the food and drug laws in the United States require extensive clinical trials of drugs before they can be approved, and that prisoners provide an ideal test group because of their particularly well controlled environment and diet. He also maintained that tests on healthy subjects are better, from both a scientific and ethical point of view, than trials on sick people. In many European countries, including Great Britain, where clinical trials are often carried out just on the sick, prisoners are seldom if ever used and Dr Stetler even went so far as to say that such testing is less scientifically rigorous.

Scientific justification and good medical practice apart, the drug companies also have a financial incentive to use prisoners for their testing. A typical payment to a prisoner for taking part in a drug trial is about \$20 or \$30 a month, which is less than one tenth of the going rate outside the prisons. Moreover, because a prisoner is less able to exercise his legal rights, the cost

of claims for damages is likely to be smaller.

Why do prisoners consent to the use of their bodies for the testing of new drugs? Therein lies the chief ethical question posed by prison research. Although low in comparison with fees outside, the \$20 or \$30 a month provides a great financial incentive to a prisoner who would normally earn only between \$2 and \$10 a month on regular prison duties. Moreover, the promise of escape from the tedium of prison life and the fact that a prisoner has little chance to exercise free will in prison surroundings also contribute to his decision to take part in trials.

With such incentives, and with such constraints on prisoners, are they in a position to give their consent to taking part in medical experiments freely, and with full understanding of the possible risks? Several witnesses at the hearings last week said that they believed not, and some recommended that an immediate moratorium should be placed on medical research involving prisoners.

Others, particularly the representatives of the Pharmaceutical Manufacturers Association, however, said that they believe that existing guidelines for the conduct of research on human subjects are sufficient to ensure good medical practice, provided that they are rigorously enforced. Drug trials involving prisoners are regulated by the Food and Drug Administration, which must ensure that the trials are carried out in accordance with the Department of Health, Education and Welfare's guidelines for human experimentation, and similarly, other medical research on prisoners funded by the federal government should conform to the guidelines (see accompanying article). But it came out in the hearings that the FDA does not have a full record of drug trials carried out in prisons, and that in any case such information would not be available to the public because it would involve trade secrets.

If a moratorium were imposed on prison research, where would the drug companies find their volunteers? Dr Capron suggested that they should look to educated people outside the prisons, who are better placed to evaluate the risks involved in, and the justification for, such experiments. And Miss Jessica Mitford, the author came up with the novel suggestion that since the stockholders of drug companies stand to benefit most from the development of new drugs, they should volunteer.

But other witnesses suggested that no new controls are necessary. As far as the right of a physician to prescribe drugs for unapproved uses is concerned, for example, Dr William Barclay, executive vice-president of the American Medical Association, argued strongly for freedom. And Dr C. Joseph Stetler, president of the Pharmaceutical Manufacturers' Association, said that no new controls are needed to guide drug trials since the present HEW guidelines are adequate if effectively enforced.

Senator Kennedy, for one, seemed convinced, however, of the need for tighter regulation of human experimentation. He took representatives of the AMA to task for failing to provide leadership in ensuring that medical experimentation is carried out ethically, and labelled many of the incidences of abuse revealed during the hearings as "utterly outrageous". Legislation bearing his imprint can be expected.

WEATHER MODIFICATION

FAS Wants the Facts

by our Washington Correspondent

THE Federation of American Scientists has called upon President Nixon to release the facts concerning US weather modification activities over Vietnam during the war, and it has also called for an international treaty banning the use of weather modification as a weapon of war. At a press conference last week, Herbert Scoville, Jun., former deputy director of the CIA, and Gordon J. F. MacDonald, who until late last year was a member of the Council on Environmental Quality, speaking for the FAS, charged that the United States has used weather modification in the Indochina war, at least experimentally.

To back up that assertion, Dr MacDonald cited a passage in the Pentagon Papers which described "Operation Popeye"—an experimental programme which enhanced rainfall over Laos in 1966. The FAS in a press release also cites the fact that on September 8 last year a commercial weather modification firm filed suit against the federal government, claiming \$95 million because the Pentagon had used a cloud-seeding device in violation of the firm's patent rights. Moreover, the federation points out that Melvin Laird, then Secretary of Defense, denied in testimony before Congress last year that weather modification had been conducted over North Vietnam, but pointedly omitted to mention the rest of Indochina.

In calling for an international treaty banning weather modification in warfare, the FAS suggests that such techniques would be "an opening wedge to the use of climate modification, the inducement of earthquakes and other

still more terrible weapons. We see geophysical warfare as a Pandora's Box, to which the seemingly inoffensive weather modification may be the disastrous key". Senator Claiborne Pell, together with 18 colleagues, has introduced a resolution into the Senate calling for an international treaty on this topic.

INDUSTRIAL RESEARCH

Optimistic Forecast

by our Washington Correspondent

THE National Science Foundation has forecast that industrially funded research and development will increase by 22 per cent between 1972 and 1975, rising from \$11,400 million last year to \$14,000 million by the middle of the decade. Based on a survey of projections made by the managers of research and development in 55 of the largest US corporations, the NSF forecast also suggests that industrial employment of scientists and engineers will increase by about 10 per cent over the same period.

The optimistic forecast given to the NSF by industrial executives "reflects a generally optimistic view of the economy", the foundation's report notes, and it is tied to expected increases in corporate earnings. During the late 1960s and early 1970s, corporate earnings declined, and companies tended to cut back in areas which would have little short term effect on profits—administration, marketing and research and development were prime candidates for the axe, the forecast suggests. The knife was not, however, applied with equal force to all items of research and development because applied research was allowed a moderate increase, while basic research was generally held back.

For the next few years, however, the National Science Foundation predicts that industrial funds for basic research will increase from \$520 million last year to about \$650 million in 1975. Of the 47 companies which offered forecasts, only one predicted a decline in spending on basic research, 13 predicted increases of up to 15 per cent, 22 reckoned they would spend between 16 and 35 per cent more, six forecast increases between 36 and 50 per cent, and five said they expected to increase spend-

ing on basic research by more than 50 per cent. The breakdown by industry is shown in Table 1.

The NSF forecast also suggests that many companies have consolidated their research and development operations during the past few years by centralizing the entire research effort, and thereby saving on such costs as library facilities and testing facilities. Moreover, although most of the company officials who responded to the survey said that expenditures required to reduce pollution have not had much effect on basic research spending, "a few of the companies noted that a significant proportion of their basic research programs was devoted to pollution control".

But the report is not entirely optimistic about expenditures on basic research, for it is pointed out that "there appears to be some disagreement regarding the value of basic research. Some companies, although continuing to perform basic research, question whether the results are worth the cost".

Short Notes

Earthquake Research

THE plan to transfer earthquake and geomagnetism research and monitoring facilities from the National Oceanic and Atmospheric Administration to the US Geological Survey (see *Nature*, 241, 362; 1973) was still stalled at the end of last week, awaiting final approval from the Office of Management and Budget. The problem is that although the Geological Survey has agreed to pick up the research, which is being dropped by NOAA because of financial stringencies, and although the National Science Foundation has agreed to put up some of the funds, the USGS does not have enough positions allocated in the 1974 budget to staff the facilities involved. Unless OMB agrees to allow the survey to have more personnel, some activities may be dropped completely.

Saturn's Rings

A RADAR scan of Saturn has produced the surprising suggestion that Saturn's rings may be composed of chunks of solid rock, and not of dust, gas or ice particles, as widely believed. The scan, carried out by Dr Richard M. Goldstein and Dr George A. Morris, Jun., of the Jet Propulsion Laboratory, produced much stronger signals from the rings than expected. The echoes suggest that the material in the rings has rough, jagged edges, and that the chunks are probably at least a metre across. Fortunately, the Mariner Jupiter-Saturn mission, which is planned for launch in 1977, does not involve passage through the rings. The scan was carried out on NASA's 64 metre antenna at Goldstone in the Mojav Desert.

Table 1 Industrial Expenditures on Basic Research

(Millions of current dollars)			
	1971	1972	1975
			(est.)
All industries	\$494	\$520	\$650
Drugs and medicines	95	105	140
Industrial chemicals	100	105	125
Petroleum	22	23	25
Electrical equipment	109	115	145
Aircraft and missiles	34	30	40
All other	134	142	175

NEWS AND VIEWS

A Classic Case of Irresponsibility

THE Metropolitan Museum of Art in New York has probably bought more than it bargained for with its recent acquisition of a splendid Greek painted vase of the sixth century BC. The museum by its purchase has undoubtedly fallen conspicuously below the standards of responsibility now expected of great archaeological institutions, and is in consequence likely to suffer a considerable dent in its prestige internationally. The resulting publicity must be causing several museums to take stock of their purchasing policies just now.

The resentment widely felt by practising archaeologists at underhand dealings on the antiquities market must be viewed against the background of the world-wide pillaging of archaeological sites, which has increased dramatically and disastrously during the past decade. In Guatemala and Mexico, for instance, looters are using power saws to cut into pieces the wonderful sculpted stelai of the Mayan civilization. Merle G. Robinson has described (*Amer. Antiquity*, **37**, 147; 1972) cases where such sculptures have been split into pieces by fire to make them more portable, and was herself held at gunpoint by looters, posing as policemen, at the site of Itzimte. The resulting fragments, even when evidently sawn from a larger monument, command thousands of dollars on the art market.

The archaeological objection to such practices is not simply repugnance at theft and vandalism. The essential point is that monuments, objects and artefacts, however beautiful they may be as art works, lose most of their meaning when divorced from the context in which they are found. This applies to a Mayan stele ripped from the site to which it belongs (and to which its inscription refers), a coin in a Roman-British settlement located by a metal detector and dug up by "treasure seekers", or a Greek vase found in an Etruscan tomb with other objects and divorced from them for sale to a "connoisseur". In each case the irreparable loss is information. The destruction is going ahead at such a rate that there are now several aspects of man's past, formerly accessible to study, about which archaeologists will always be ignorant. To the irreparable damage in Mesoamerica must be added the archaeological rape of Cyprus, the ransacking of the Cycladic cemeteries of Greece, and especially the continuing plunder of the Etruscan cemeteries of Italy—the centre of an extensive antiquities trade for more than a century.

The archaeological world has now realized that policing the sites, although desirable, is not everywhere practicable. The solution must come from a new sense of responsibility among museums and private collectors. Pieces should be purchased only when their legitimate provenance is securely known, whether from authorized methodical excavation or from existing, recognized (and published) private collections. Anybody who buys antiquities in different circumstances is sustaining the market in plundered material. The Unesco draft convention on the safeguarding of archaeological sites (*Antiquity*, **45**, 246; 1971) sets clear guidelines, and lead-

ing institutions, such as the University of Pennsylvania Museum, and Harvard University (*Antiquity*, **46**, 90; 1972) have drawn up conventions to ensure that their purchases do not directly or indirectly support looting or the illicit export of antiquities from the country of origin.

It is in this context that the Metropolitan Museum's purchase, for a reported \$1,000,000, of an Attic red-figure vase, dated to about 510 BC and depicting a scene relating to the death of Sarpedon by the painter Euphronios, must be judged. It was acquired from an American dealer resident in Rome, who has in the past been charged with the violation of antiquities laws. He, in turn, claims to have obtained it from an Armenian antiquities dealer in Beirut (*The Observer*, February 25, 1973), but the vase has not previously been described, and there are grounds for suspecting it to have been illicitly excavated in Italy during the past five years.

That the museum should buy "the best Greek vase there is", in such circumstances and for a sum far in excess of any previously paid for a Greek vase, is scandalous enough; reminiscent, indeed, of the purchase by the Boston Museum of Fine Arts of a golden treasure (see *Nature*, **232**, 515; 1971) which had obviously been illegally exported from some east Mediterranean land.

The attitude of the museum's officials is yet more shocking. Dietrich von Bothmer, the curator of Roman and Greek art and an internationally recognized authority, is credited in *The Times* of February 20, 1973, with the following statement:

"I want to know whether it is genuine or fake. Its intermediate history is not important to archaeology. Why can't people look at it simply as archaeologists do, as an art object?" When asked whether he suspected that the vase could have been smuggled out of Italy recently, Mr von Bothmer answered: 'I am not suspecting anything. The thing I was concerned about was whether the object was genuine, whether the object was worth the money we spent on it.'"

The pronouncement, echoing some of the less scrupulous nineteenth century "art lovers", that the circumstances of archaeological finds may be dismissed as "intermediate history", must rank as a classic of irresponsibility. More seriously, the admission of such a view—whatever the origin of the Euphronios vase itself—saddles the Metropolitan Museum of Art with a substantial measure of responsibility, albeit perhaps indirect, for the present looting and destruction of archaeological sites in the world at large.

The contumely of the scientific community in general, coupled with strong public pressure (for the scandal has been widely reported in the press), may yet bring the officials of the Metropolitan Museum to appreciate the magnitude of their present irresponsibility and the discredit which they bring upon the world of art scholarship.

From our Archaeology Correspondent

Sudden Events

THE importance of sudden events has become increasingly evident to astronomers in recent years. Perhaps such occurrences are noticed most commonly in some of the quasars. Typically what happens is that an intense component of radio emission, with a very small angular diameter, becomes visible for a period of a few months. During this time it contributes an appreciable proportion to the energy output of the whole quasar at radio frequencies. The radio emission at a given frequency first rises with time, reaches a maximum, and then decays; the higher frequency components achieve their maximum intensity before the lower frequency components. The whole effect can be explained beautifully on a model which was proposed by van der Laan several years ago. According to his ideas the radiation is generated in a giant bubble consisting of relativistic plasma mixed up with a magnetic field. As the bubble expands, the electrons lose energy and the magnetic field strength decreases. This gradually shifts to lower values both the frequencies at which the electrons emit most effectively and those at which the bubble is just transparent.

The model has one drawback, though. It says nothing about the way in which the relativistic plasma is given its energy in the first place. This is rather an important point, for the total energy required by the bubble depends very sensitively on the way in which it is started off. The early phases of its life are the most expensive in energy. But so far there are no observations of such a relativistic bubble in a quasar at the beginning of its life. In any case it may well be that the early phases of its evolution take place under conditions of such high density that it is impossible to observe directly just what is going on.

It is therefore fortunate that just over six months ago an outburst occurred in our Galaxy which looks very much like a small scale replica of such a sudden event in a quasar. The occasion was first observed on September 2, when the intensity of the radio emission from the X-ray source Cygnus X-3 suddenly increased by some orders of magnitude over its usual quiescent value. The subsequent events were comprehensively described in the October 23 issue of *Nature Physical Science*. It was found that the later evolution of the Cygnus X-3 outburst could be very well accounted for by the same model that van der Laan had proposed for sudden events in quasars (although the physical parameters such as magnetic field strength and total energy content had to be scaled down to the more modest proportions of this particular explosion). But it turned out that the observations made on the first day after the outburst did not fit the model too well. In particular there were oscillations in intensity at the higher frequencies that could not possibly be explained.

In an article on page 173 of this issue of *Nature* an attempt is made by Peterson to improve understanding of the early phases in the development of the bubble. He makes the modification that the relativistic plasma is not injected into the bubble all at once, but over a period of about a day. He postulates a particular form for the law governing the injection of plasma and then varies a

set of parameters until he obtains the closest possible fit between his model and the observed evolution of the spectrum of the radio outburst. His conclusion is that the injection continued for about 30 h and that the minimum size of the bubble was about 10 AU.

Now this is most interesting, but also most tantalizing. How does all this agree with what is known about X-ray sources? Observations show that the X-ray emission from these sources often has quite short period oscillations, of the order of seconds. In the usual way one concludes that the underlying object must therefore be very compact; the only likely candidates are neutron stars or black holes. Somehow the release of the energy must have occurred in the underlying object. The energy was then propagated away from the source; later it was given to the radio bubble, which was observed after September 2. But neutron stars and black holes do not have dimensions as large as 10 AU; an estimate of 1 to 10 km would be much nearer the mark. There are therefore two problems: where did the energy come from, and how was it transmitted to the much larger region where the radio bubble began its existence?

Most probably the source of the energy is connected with the release of gravitational energy. It will be interesting to study how this happened, particularly if it turns out that the central object of Cygnus X-3 is actually a black hole. The transfer of energy, one would guess, must have occurred by some electromagnetic process, but under rather unfamiliar conditions. A reasonable picture might be as follows. Suppose that a mass of plasma falls towards a black hole or onto the surface of a neutron star. Suppose further that a quantity of magnetic flux is linked with the plasma. During the final stages of the collapse the magnetic dipole moment due to this flux will undergo rapid changes. One consequence is the emission of low-frequency electromagnetic radiation: the intensity of the emission increases up to the moment when the plasma gets lost in the black hole or the neutron star. If the plasma cloud has angular momentum the process may be augmented by the emission of low-frequency radiation from a rotating dipole, rather as is the case in some theoretical model of pulsars.

In either case one would expect a radiation field with characteristic frequencies in the region of 10 kHz. This radiation field has waves of low frequency but it carries much energy. Its mode of propagation through any ambient plasma is, however, not well understood; the waves have such a large amplitude that they cause large variations in the mass of the charged particles of the medium through which they are travelling. Any theoretical attempt at understanding this process leads at once to a difficult non-linear problem, whose solution is known in only a few special cases. But it does seem likely that in sudden events of this kind the relativistic electrons in the radio bubble have been energized by interaction with a set of low-frequency waves.

It is quite natural therefore that strenuous attempts should be made to understand these electromagnetic phenomena. The outburst of Cyg X-3 provides the best set of observations from which to derive data about the actual behaviour of such waves. The analysis by Peterson shows how one can extract much additional information from the records of the event.

F. D. K.

The Problem of Pain

It is relatively rare for scientific theory to lead directly to a new clinical procedure. The use of electrical stimulators on patients with intractable pain, however, is a case in point. These devices represent a radical reversal of the surgical approach to the problem of the patient who is left with severe chronic pain after damage to peripheral nerves or to the spinal cord. For whereas the aim of surgery is to destroy the nerve tract through which the pathological signals are transmitted to the brain, the idea behind the stimulators is to increase activity in the remaining normal nerve fibres.

This therapeutic approach arose from the Melzack-Wall gate control theory of pain, which states that the transmission of the sensation is controlled by the balance of activity in small diameter, slowly conducting fibres and large diameter, fast fibres entering the spinal cord. According to gate control theory, tonic activity in the small fibres which mediate pain is normally blocked at the first synapse by the activity of the large fibres which mediate mechanoreception, as well as by descending fibres from higher brain centres. The blockage can be overcome by very intense stimulation of the small diameter afferents, such as that which would result from tissue damage (Melzack and Wall, *Science*, **150**, 971; 1965).

The electrical stimulators are designed to excite the large diameter fibres, which have a relatively low threshold, without increasing activity in the higher-threshold small fibres, and thus to close the spinal "gate". They can now be surgically implanted in patients in the form of radio receivers, either close to a deep peripheral nerve or on the dorsal columns of the spinal cord itself, where stimulation is presumed to activate large diameter afferents antidromically (that is, by firing the axons passing on to the brain backwards, to close the gate).

In the United States, several hundred of these devices are now in use, and trials have recently begun in Britain, notably at the Institute of Neurology in Queen Square. The results have been mixed. At best, a short period of stimulation at intervals brings the patient total relief from pain. At worst, it has no effect at all. As far as can be judged, the clinical results seem to justify further trials at least. But do they vindicate the theory on which the therapy is based?

First, what is the explanation for the persistence of the analgesic effect, sometimes for several hours, after stimulation has stopped? Wall and Sweet (*Science*, **155**, 108; 1967) have suggested that the spontaneous activity of the small fibres may take time to reopen the gate. This would be consistent with the theory, but is not specifically predicted by it. Second, what is the effect on normal pain—for example pinprick—of stimulating the large diameter fibres? Wall and Sweet tried this on themselves with external stimulators and reported that pinprick in the analgesic areas did not feel sharp, though ordinary nonpainful sensation was unaffected. The accounts of patients on this point, however, are often conflicting and the issue is clearly complicated by the subjective nature of such judgments.

Indeed, the subjective nature of pain itself tends to confuse discussion of its possible mechanisms. While

nobody would now dispute that painful sensation is mediated by specific anatomical pathways, the uncomfortable fact remains that severing these pathways does not always relieve pain. The arguments reach their metaphysical zenith when the surgeon, as a last resort, cuts the pain-carrying fibres between the thalamus and the frontal lobes of the cerebral cortex. The patient still feels the pain, but it no longer appears to worry him. The surgeon has apparently succeeded in eradicating the affect; hardly an anatomical concept.

The great advantage of gate control theory is that it attempts to explain the phenomena in purely neurophysiological terms at a manageable level of the nervous system and is therefore potentially testable. Attempts to identify the neurophysiological substrate for gate-controlled pain perception have thrown up several candidates for the spinal pathway involved, and have led to arguments about the circuitry of the gate(s) which remain inconclusive.

Wall and colleagues (*J. Physiol.*, **199**, 51; 1968), recording from the axons in the dorsolateral tract (DLT) of the cat spinal cord, found that they were driven both by small nonspecific afferents and by large mechanoreceptor afferents, which produced the expected facilitation of transmission in the case of the first, and presynaptic inhibition in the case of the second. Other workers, notably Perl and his colleagues at North Carolina, have fixed upon different pathways in which a proportion of the fibres can be driven by afferents which seem to be specific to noxious stimuli, but which do not seem to be subject to gate control, or at least not in the manner proposed by Melzack and Wall.

Dr P. R. Burgess, of the University of Utah, described at a recent conference of the Society for Neuroscience in Houston a paradoxical system in which noxious stimuli apparently close the gate. Small fibres responding to noxious stimuli are presynaptically inhibited by large mechanoreceptor fibres, as predicted, but when the stimulus is increased to noxious intensities, instead of breaking through the inhibition, they are even more firmly inhibited.

The most recent of the putative pain pathways is proposed by Dr B. Pomeranz, on the basis of single unit recordings from the ventrolateral tract (VLT) of the spinal cord (*Brain Res.*, **50**, 447; 1973). Thirty per cent of the fibres recorded by Pomeranz responded to noxious stimuli only; transmission, however, was neither facilitated presynaptically by stimulation of small diameter afferents, nor inhibited by large diameter afferents. On the basis of the proportion of fibres driven by noxious stimuli, Pomeranz reasons that the pathway is likely to be involved in the transmission of pain, but there is no evidence that it is gate-controlled.

A recurrent difficulty with research on the neurophysiology of sensory afferents is that their responses are profoundly influenced by general factors such as the condition of the animal from which the recordings are made. Such factors have often been called to account for discrepancies in the findings of different groups working on the same systems.

There is no doubt that the theory of pain as proposed by Melzack and Wall has been the basis for fruitful experiment both in the laboratory and in the clinic. One of the consequences of the work inspired by the theory has been to show where the theory is incomplete.

BRAIN DEVELOPMENT

Cerebellar Guidelines

from a Correspondent

THE mammalian brain is a structure of such complexity that the discovery of the principles governing its development poses a major challenge to biologists. One particularly productive approach to this problem is that adopted by Sidman and his colleagues at Harvard University. They have been studying, in mice, the effects of single gene mutations on neural structure, concentrating particularly on the cerebellum. This part of the brain is a beautifully ordered neuronal structure which is closely implicated in the fine coordination and control of muscular activity. A mutant animal with an abnormal cerebellum displays characteristic signs of muscular incoordination, low tone in the muscles and frequently a tremor. The various types of mutant have acquired evocative names such as "reeler", "swayer", "staggerer", "weaver" and "nervous".

In a recent report Rakic and Sidman (*Proc. US Nat. Acad. Sci.*, **70**, 241; 1973) analyse the cerebellar defect in the mutant weaver. In the homozygous animal there is, by the age of three weeks, an almost complete absence of one cell type—the granule cells. In the adult cerebellum the granule cell lies beneath the layer of Purkinje cells—those large cells whose axons constitute the sole output from the cerebellar cortex. The granule cells receive their input from mossy fibres, one of the two types of afferent fibres to the cerebellum, and send their axons to specialized spines on the dendrites of Purkinje cells. The granule cells are thus an essential link in one of the principal neuronal circuits of the cerebellum and it is not surprising that in their absence gross signs of cerebellar dysfunction are apparent.

What is the cause of the granule cell death in homozygous weaver mutants? Is the demise of the granule cell a primary effect of the defective gene or a secondary phenotypic expression of some more elusive primary genetic effect? During normal development the precursors of the granule cells travel over the surface of the brain to the surface of the cerebellum, where they then undergo massive proliferation. The daughter granule cells then migrate from the cerebellar surface through a dense meshwork of cells and cellular processes to assume their adult position deep in the cerebellum. In homozygous weaver the granule cells die at the cerebellar surface and hence no migration takes place. Rezai and Yoon (*Develop. Biol.*, **29**, 17; 1972) demonstrated that in weaver heterozygotes the granule cells proliferate normally but the daughter cells migrate

more slowly to their deep position. They suggested that in the homozygote cell death is secondary to a failure of migration rather than the reverse.

Rakic (*J. Comp. Neurol.*, **141**, 283; 1971), in an elegant electron microscope study of the developing monkey cerebellum, showed that throughout the entire extent of its difficult transcerebellar passage the migrating granule cell is intimately apposed to the process of a radially orientated glial cell (Bergmann cell). It was suggested that these glial processes act as necessary guidelines for the journey of the developing neurone, and in view of Rakic's discovery (*J. Comp. Neurol.*, **145**, 61; 1972) of a similar neurone-glial relationship in the developing cerebral cortex, it seems possible that such glial guidance is a fairly general phenomenon. Rakic and Sidman decided to investigate the relationship between granule cells and Bergmann glial cells in weaver mice to see if some abnormality in this relationship is the cause of the failure of the granule cells to migrate.

Rakic and Sidman found that in homozygous weaver mice the radial processes of the glial cells, although not entirely absent, are very rare. In the heterozygote, which does not display clinical symptoms, Bergmann glial processes are present but abnormal, the

distal processes being enlarged, irregular and vacuolated. This reduced effect in the heterozygote is part of the basis for the authors' conclusion that, although neuronal death is the most prominent and clinically relevant phenotypic expression of the weaver mutant, the Bergmann glial abnormality may actually be closer to the primary cellular target of the *wv* genetic locus.

The importance of normal cell migration in brain development is also demonstrated in "reeler" mice where defective migration leads to disordered neural structures. In reeler, however, it is proving more difficult to identify the primary genetic defect (Caviness and Sidman, *J. Comp. Neurol.*, **145**, 85; 1972; and **147**, 235; 1972). In "staggerer", on the other hand, the phenotypic expression of the defect consists of the absence of a specific synaptic relationship, that between the granule cell and the Purkinje cell dendrite. All other cerebellar synaptic relationships are present. Sidman argues that the primary defect, in this case, lies in the Purkinje cell itself.

A potentially very powerful complementary approach to cerebellar development is offered by Altman and Anderson (*J. Comp. Neurol.*, **146**, 355; 1972). Controlled X-irradiation at particular post-natal periods can destroy selectively certain neuronal populations

What is the Origin of RD114 Virus?

RD114 VIRUS has attracted much attention recently because it has the characteristics of C-type RNA tumour virus and is released from human tumour cells, albeit human cells that have been passaged *in vitro* and in a foetal cat. The central question, of course, is what is the origin of RD114 virus? Is it a cat virus that infected the human cells during their passage in the kitten, or is it a human virus the replication of which was induced by the passage of the human cells in a kitten?

As has been shown by McAllister and his colleagues, who discovered RD114 virus, and by others, who have helped to characterize it, the antigens and the reverse transcriptase of RD114 virus particles are not closely related to their counterparts in either primate or feline C-type viruses. In an attempt to rule out the possibility that RD114 virus is merely feline leukaemia virus modified by passage in human cells, McAllister *et al.* performed the set of experiments that are reported in *Nature New Biology* next week (March 21).

McAllister *et al.* infected human RD cells, that do not release any virus, with either feline leukaemia virus or the Kirsten strain of murine sarcoma (this latter virus was obtained from rat cells and it grows well in both rats and human cells) and then assayed various

properties of the progeny virus particles to see if they had been modified by passage in the human RD cells. McAllister *et al.* also investigated the properties of the infected and transformed RD cells. As far as could be judged from the results of a variety of tests, feline leukaemia virus particles from infected RD cells were identical to feline leukaemia virus particles from cat cells. Likewise the Kirsten murine sarcoma virus was not detectably altered by passage in RD114 cells. This indicates that RD114 virus is distinct from feline leukaemia virus and it is not simply a feline leukaemia virus somehow modified by passage in RD human cells.

McAllister *et al.* hint at the possible origin of RD114 virus. Apparently Todaro and his colleagues have induced from cat cells a virus closely resembling RD114 virus. It may be therefore that RD114 virus is a feline C-type virus quite distinct and unrelated from the already characterized feline sarcoma and leukaemia viruses. As they say, "The cat may be the first species found to have two distinct unrelated C-type viruses"; this is interesting but is also a great disappointment for anybody who hoped that RD114 virus might be the first human C-type virus to have been isolated.

and the effects on cerebellar organization of the deletion of different cell populations by experimental or genetic means can be compared. These ongoing studies are providing invaluable insights into the mechanisms of brain development.

PROTEINS

Sifting the Subunits

from our Molecular Biology Correspondent

THIS week some *bonnes bouches* for collectors of the odd in the way of protein structures. Some proteins, on no very obvious teleological grounds, exist under physiological conditions in very large aggregates, containing many subunits. One of the first cases to be recognized was haptoglobin, a serum globulin, which has the function of absorbing any haemoglobin that is released into the plasma. There are three familiar genetic variants of human haptoglobin, one of which (Hp 1-1) is electrophoretically homogeneous, whereas the others, Hp 2-1 and Hp 2-2, take the form of an apparently limitless series of components of progressively lower mobility in the electrophoretic gels. More than a dozen zones can often be resolved, and these are now recognized as a set of linear polymers, which can be separated on denaturation and reduction into two types of chain, α and β , the α chain being characteristic of the haptoglobin type, the β chain common to all three. Just what the relation is between the members of the family of oligomers—for example, whether they are built up by successive addition of $\alpha\beta$ units, or of tetramers, or, as has been suggested, by repeated dimerization—has hitherto been in doubt. Now, however, Fuller *et al.* (*Biochemistry*, **12**, 253; 1973) seem to have settled the question.

Their preparation of haptoglobin 2-2 showed fourteen resolved zones in polyacrylamide gels and the first eight of these were isolated by preparative electrophoresis. In the absence of a reducing agent, the polymers do not dissociate in sodium dodecyl sulphate, and so detergent-gel electrophoresis could be used to give a first estimate of the molecular weights of the resolved members of the series. The first zone had a mobility corresponding to a molecular weight of some 200,000, which is consistent with an $\alpha_3\beta_3$ structure, the α chains with a molecular weight of 17,000 and the β chains 40,000. The apparent molecular weight increment between successive zones was constant, and corresponded to the addition of an $\alpha\beta$ unit at each step. The components from 2 to 5 were examined by sedimentation equilibrium, and the inferred molecular weights from the electrophoresis experi-

ments were found nearly enough correct. The stoichiometry was more firmly established by amino-acid analysis and by end-group determination. Both confirmed that α and β chains were present in equimolar concentrations in all cases. Now it has been known for some time that the chains of the basic $\alpha\beta$ unit are united by disulphide bonds, and Fuller *et al.* now also show that disulphide bonds likewise secure these units to each other in the polymers, because electrophoresis in the presence of very low concentrations of mercaptoethanol reveals the progressive degradations of polymer 5, for example, to a mixture of components 2 to 5, number 4 being formed first. The $\alpha\beta$ subunits do not come apart, and the α - β disulphide bonds can, it seems, be reduced only under more drastic conditions. Evidently, therefore, the components of the polymerizable genetic haptoglobin forms are assembled by linear addition from a pool of $\alpha\beta$ units.

In unfolding the absorbing story of the enzymatic control of glycogen

metabolism, Krebs and his colleagues have paused to examine the structural character of the phosphorylase kinase, which is responsible for the conversion by phosphorylation, of glycogen phosphorylase *b* to phosphorylase *a*. The activity of the phosphorylase kinase is itself controlled by cyclic AMP-dependent protein kinase, which catalyses its phosphorylation. The phosphorylase kinase emerges as a complicated enzyme with some curious properties. In the first of a set of three articles, Hayakawa *et al.* (*ibid.*, 567) describe the isolation of the protein in a high state of purity, having eliminated an aggregated fraction present in earlier preparations. The enzyme, when thus purified, has a sedimentation coefficient of 26S and a molecular weight, by sedimentation equilibrium, of 1.3×10^6 . In sodium dodecyl sulphate it dissociates, and gives rise to three components with apparent molecular weights of 118,000, 108,000 and 41,000, which are termed the A, B and C chains. From the apparent concentrations of these components, the authors infer that the

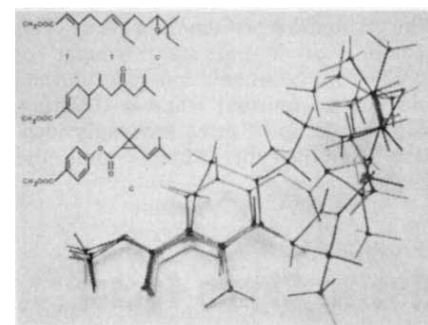
Structure and Activity of Juvenile Hormone

MANY attempts have been made during the past few years to define the molecular characters that determine the juvenile hormone activity of the rather diverse chemicals which can produce these morphological effects (*Nature*, **221**, 190; 1969). In the first place the molecule must be neither too long nor too short: active substances have about fourteen carbon atoms in the chain length. They must not be too polar, nor must they be wholly paraffinic. General molecular configuration determined by *cis* or *trans* bonding along the chain is highly important, but no molecular shape that gives predictable effects has been defined.

The problem is complicated by the diverse effects of synthetics in different groups of insects. Although the natural juvenile hormone as originally isolated from the cecropia silkworm seems to have universally high activity, even the simple straight chain compound dodecyl methyl ether is quite active in Lepidoptera, though very weak in activity in other groups; and "juvabione", the methyl ester of todomastic acid from balsam fir, which is intensely active in plant bugs of the family Pyrrhocoridae, seems to be without effect in any other insects.

In next Wednesday's *Nature New Biology* (March 21), Punja, Ruscoe and Treadgold report on a new group of non-terpenoid compounds, esters of chrysanthemic acid, which possess a high order of juvenile hormone activity. These also were found to be active only in the pyrrhocorid bug *Dysdercus*; but the communication brings out clearly

that activity is largely determined by the configuration at the C_1 end of the molecule where the most active mimics have a terminal carboxy alkyl or similar group conjugated with a double bond held *trans* to a long alkyl chain. As clearly shown in Dreiding molecular models the most active chrysanthemates, the principal cecropia hormone and juvabione all have closely similar configurations which are superimposable over this region (see figure). Extensive changes in other parts of the molecule seem to be much less significant.



These results do not explain changes in overall and species-related activity which are associated with small variations in structure. There is no indication as to why the effect of chrysanthemates is specific for Pyrrhocoridae, nor for the increased activity which is conferred by a methyl side-chain at C_3 and by methyl (as compared with ethyl) esters. But the molecular models demonstrate the importance of the spatial relationships in the terminal groups of juvenile hormone and its mimics.

native enzyme has the structure $A_2B_2C_2$.

The A and B chains can be separated on a preparative scale from the smaller C chains by chromatography in sodium dodecyl sulphate solution (Hayakawa *et al.*, *ibid.*, 574) and the approximate molecular weights were confirmed by sedimentation equilibrium. The activation of the enzyme by incorporation of phosphorus from labelled ATP was found to implicate both the A and the B, but not the C, chains. Phosphorylation of the B chains occurred much more rapidly, but the activity continued to rise as incorporation progressed to the A chains. Activation can also be occasioned by exposure of the phosphorylase kinase to trypsin, and this again affects only the A and B subunits, both of which are broken down to fragments of lower molecular weight. Hayakawa *et al.* hazard the view that C, which is unaffected by any of these treatments, may be the catalytic subunit, which is regulated by A and B. Moreover, the trypsin-activated enzyme can, as Graves *et al.* (*ibid.*, 580) report in the third article, be dissociated in the presence of ATP, by a slow process to smaller species, sedimenting at 9S and 16S, which possess activity, and in the smaller of which no part of the A subunit can be detected. The native, undigested, kinase cannot be made to dissociate under any but denaturing conditions, yet it seems that the very large cluster of subunits that comprises the native enzyme is not a condition for enzymatic activity.

Another curiosity, and the subject of a painstaking study by Roseman and his colleagues, is a bacterial protein involved in the transfer of phosphorus to lactose (Hays *et al.*, *J. Biol. Chem.*, **248**, 941; 1973). The sites of phosphorylation are histidine residues. This protein has a molecular weight of 35,000 by sedimentation equilibrium, and has an unusual trimeric structure, being made up of three seemingly identical subunits of 12,000 molecular weight apiece.

TRANSCRIPTION

Elusive Sigma Factor

from our Cell Biology Correspondent

THE hopes of divining how RNA polymerase knows which DNA to transcribe and which DNA to leave untranscribed, that were raised among molecular biologists two and three years ago by the discovery of a subunit of *Escherichia coli* RNA polymerase called sigma factor, have slowly evaporated. And the article by Greenleaf, Linn and Losick in the current issue of the *Proceedings of the National Academy of Sciences* (70, 490; 1973) seems like a haunting voice from the

past. During the heydays of sigma factor Losick and his colleagues confidently anticipated that during the sporulation of the bacterium *Bacillus subtilis* the change in pattern of transcription of the bacterial DNA would prove to result from changes in the RNA polymerase molecule, and at that time (1969) it seemed plausible to suggest that the sigma factor responsible for programming the transcription of genes expressed during the vegetative phase of the life cycle was replaced by a new sigma factor programming the transcription of different genes expressed specifically during sporulation.

Losick and his colleagues found that the vegetative sigma factor is indeed lost early during sporulation, a fact which could account for the turnoff of ribosomal RNA synthesis and the failure of the sporulating cells to support the growth of phage ϕ . They also found that one of the other polypeptide chains of the vegetative enzyme (the β subunit) is replaced by a smaller polypeptide during sporulation. Egged on by these discoveries, and in particular the loss of the vegetative stage sigma factor at the start of sporulation, Losick and his colleagues began to search for the putative new sigma factor characteristic of the enzyme in sporulating cells. The report in the February issue of the *Proceedings* describes the results of this search which, frankly, are disappointing.

If a new sigma factor is made during sporulation the obvious place to look for it is in the RNA polymerase from sporulating cells, of which the factor

should be a component. Greenleaf *et al.* therefore prepared antibody against the core polymerase of vegetative cells (core polymerase lacks sigma factor). They then challenged RNA polymerase from sporulating cells with the anti-core polymerase antibody and found that a polypeptide with a molecular weight of about 70,000 coprecipitated with the polymerase from sporulating cells. Clearly this coprecipitating polypeptide not present in the vegetative core enzyme might well be a sporulation sigma factor. Greenleaf *et al.* therefore purified the 70,000-dalton polypeptide and established that it binds specifically to core RNA polymerase, a property which a putative sporulation sigma factor must have; depending on the conditions, 0.3 to 2 molecules of 70,000-dalton polypeptide bind to each core polymerase. Furthermore, this polypeptide first appears about 3 h after the start of sporulation and persists for about at least a further 3 h and it cannot be detected in RNA polymerase extracted from a mutant of *B. subtilis*, *rfr10*, which cannot sporulate and which is rifampicin resistant; cell extracts from this mutant also lack the 70,000-dalton polypeptide.

With such a body of circumstantial evidence it must have been hard for Greenleaf *et al.* to resist the temptation to send out for a corkscrew, but the celebrations would have been premature, for the last sentence of their report reads: "Attempts to demonstrate a role for the 70,000-dalton binding protein in the transcription of sporulation genes have not yet been successful."

Hatched from the Same Egg

THE evidence, based on sequence homologies, that several proteins have a common evolutionary origin brings a measure of conviction. Is the same true of non-translated gene products, namely ribosomal and transfer RNA? Mullins *et al.* have investigated this question and in next Wednesday's *Nature New Biology* (March 21) they report their comparison of the pre-modified sequences of non-informational RNAs including twenty-two tRNAs and 5S RNA.

Mullins *et al.* found that tRNA^{trp} and tRNA^{glu} from *Escherichia coli* show a remarkable homology with 5S RNA from the same species and that several other tRNA sequences are only a little less homologous. Although several insertions and deletions are required to make these homologies manifest, they are apparently well above chance expectation. Nevertheless they show a peculiar pattern—which Mullins *et al.* term "displaced linear homology"—in that the first half of the tRNA sequences are homologous with the last third of the 5S sequence and the second half of

the tRNA with the first third of the 5S. Moreover, the extra sequence of forty-one nucleotides at the 5' end of the precursor form of tRNA^{trp} shows homology with the middle third of the 5S RNA sequence.

Mullins *et al.* interpret these results ingeniously, using the observation of Brownlee, Sanger and Barrell (*Nature*, **215**, 735; 1967) that for *E. coli* 5S RNA the first nine residues show homology with the last nine and that region 10–60 is homologous with region 61–110; in other words, the molecule has a palindromic structure with the pattern ABBA. Mullins *et al.* postulate a proto-non-informational RNA consisting of about sixty residues with the pattern AB. They suggest that this gave, by processes of partial gene duplication, a sequence first with the structure ABB and then with the structure ABBABB. This, they suggest, gave by a similar process a sequence with the structure ABBA corresponding to 5S RNA and alternatively a sequence BAB, which after truncation would correspond to tRNA.

Until some direct evidence, either from *in vitro* experiments or from studies of mutant strains of *B. subtilis* carrying conditional lethal mutations in the structural gene specifying the 70,000-dalton polypeptide, is obtained the role of this polypeptide in the specificity of transcription during sporulation must remain uncertain.

LEUKAEMIC CELLS

Mutagenic Polymerase

from our Cell Physiology Correspondent

REPORTS about the physiology of various tumours and more particularly about the relationship between the host and the malignant cells are now legion, but although knowledge of the molecular biology of malignancy is fundamental to its control, information on this point is sadly lacking. It is true that many workers are investigating reverse transcriptase, but there are innumerable other facets of the molecular workings of these cells which also warrant study.

Springgate and Loeb have started on a new track, for they are now trying to determine whether DNA synthesis in malignant cells is less accurate than that of normal cells. The idea seems to be something of a shot in the dark, but in their recent report (*Proc. US Nat. Acad. Sci.*, **70**, 245; 1973) they show that the cells from four patients with acute lymphatic leukaemia have a DNA polymerase which is considerably less exact and makes a far greater number of mistakes when copying a template than does the DNA polymerase from normal human lymphocytes.

After removal of indigenous DNA the accuracy of synthesis was assessed by determining the proportion of radioactively labelled dGTP or dCTP incorporated during replication of a synthetic poly(dA-dT) · poly(dA-dT) template. The enzymes from leukaemic cells apparently lack the fidelity of those from normal lymphocytes, for the proportion of cytidine residues in DNA synthesized by polymerases from cells of patients with acute lymphatic leukaemia was some ten times higher than that made by DNA polymerases from normal lymphocytic polymerases the mic polymerases the level of errors lay between 1 in 250 and 1 in 850, with normal lymphocyte polymerases the error frequency was of the order of 1 in 2,000 to 1 in 30,000.

Control experiments indicate that the dCTP really is incorporated into the polynucleotide chain and is not merely attached to it non-specifically. In identical conditions the *Escherichia coli* enzyme was found to have an error frequency somewhat lower than 1 in 100,000 and that of T4 phage was in the region of 1 in 10,000; these values agree very closely with those found by

other authors. Other simple experiments also suggest that the observation is not an artefact, for the addition of cold, unlabelled dCTP to the nucleotide pool reduced the proportion of label incorporated into the freshly synthesized polymer and the requirements of the assay system for Mg^{2+} , template, nucleotides and enzyme are exactly the same for incorporation of both correct or incorrect bases. If the correct bases, dATP and dTTP, are labelled with ^{32}P and the incorrect base, dCTP, with 3H , then the ratio between 3H and ^{32}P remains the same, irrespective of both the amount of enzyme protein added to the reaction mixture and also to the time over which the reaction is measured.

Springgate and Loeb believe these experiments indicate that the incorrect dCTP is physically incorporated into the replicating polynucleotide; much stronger support for this contention comes from two further experiments.

In the first experiment, caesium chloride density gradients showed the product of the polymerase reactions to band in the position expected for a poly(dA-dT) · poly(dA-dT) and, as would also be expected if the dCTP were an integral part of the molecule, 3H -dCTP was found in exactly the same band. Again, if the freshly synthesized polynucleotide was labelled with ^{32}P -dTTP and 3H -dCTP and then sequentially hydrolysed with snake venom phosphodiesterase the release of the two bases closely paralleled one another. These results indicate that the cytosine residues are incorporated into the DNA and that they are evenly distributed.

Apparently it was not possible to assess the extent of inaccuracy using a poly(dG) · poly(dC) template because the level of infidelity was too low to allow for accurate measurement. Results with the poly(dA-dT) · poly(dA-dT) template strongly suggest, however, that these acute lymphatic leukaemic cells

Adherent Cells and B Cell Immunity or Tolerance

FOLLOWING the realization that many immune responses cannot be thought of in terms of the interaction of antigen with a single species of lymphocyte, cellular immunology has entered a more realistic but more complicated phase of analysis. Broadly there are three kinds of cell known to be involved—T lymphocytes from the thymus, B lymphocytes from the bone marrow (or bursal equivalent) and adherent cells which also derive from the bone marrow but which are probably macrophage-like cells rather than lymphocytes.

All three sorts of cell are thought to have specific and non-specific parts to play in an immune response. The favourite notion at present is that specifically-activated T cells synthesize both non-specific and specific factors as a result of contact with specific antigen. The specific factor, which is thought to be an immunoglobulin referred to as IgT, becomes bound to the surface of a macrophage where in turn it binds antigen. The antigen-IgT complex can stimulate B cells to produce the specific antibody. It is possible that the macrophage stimulated by antigen-antibody complexes and the activated B cell in their turn secrete non-specific and perhaps specific (in the case of B cells) regulators of the cellular consortium. In next Wednesday's *Nature New Biology* (March 21), Feldmann illustrates how the presence of an adherent cell can determine whether B cells are induced to synthesize a specific antibody by activated T cells or become specifically tolerant.

All Feldmann's results relate to experiments performed *in vitro* and carry

the limitation that the antibodies produced are IgM only. The crucial part of the study is that activated thymocytes in contact with DNP (dinitrophenyl) conjugated to the activating antigen (fowl gamma globulin) liberate into the supernatant a factor which can induce spleen cells previously primed *in vivo* to DNP flagellin and in the presence of DNP-POL (POL is polymerized flagellin) to produce anti-DNP antibody as measured by the Jerne technique. If adherent cells are removed from the spleen cell population before incubation with the supernatant, then little anti-DNP antibody but anti-POL antibody is produced. Feldmann's interpretation of this experiment is that IgT-DNP complexes can specifically immunize primed B cells when presented to the B cells by an adherent cell population, but can also specifically tolerize if they come in direct contact with the B cells.

Feldmann feels that these experiments have an *in vivo* parallel in those situations in which large numbers of activated T cells can suppress immunity. He distinguishes three phases in an immune response; first, an exponential phase in which the amount of IgT is less than the number of receptors available on macrophages and therefore in the absence of unbound IgT-antigen complexes immunity will develop; second, a plateau phase during which complexes and receptors are present in roughly equal numbers and in the absence of free complexes only immunity can result; and third, a tolerance phase in which free IgT complexes are present and these effectively tolerize B cells.

do have some defect in their ability to replicate DNA with any accuracy. Does this result from errors in synthesis or through a failure of the nuclease to "edit" any errors introduced during DNA synthesis? Other questions concern the origin of the faulty polymerase. Is this of viral origin, or does it reflect the presence of an altered lymphocyte polymerase which is defective in base selection? On a more positive note, it is certain that such errors will enhance the mutation rate of these leukaemic cells and it is highly probable that this is responsible for the increasing variation which occurs during their proliferation.

The selective advantage which such random genetic mutation would confer on leukaemic cells is obvious, and what one now needs to know is whether DNA polymerases from the cells of other tumours show the same propensity for mis-replication. Is there, in fact, any relationship between mis-replication of DNA and a viral or non-viral origin of the malignancy?

EARTH MODELS

New Oceanic Model

from our Geomagnetism Correspondent

THE classical Earth models were seismically based on body wave travel-time data. In recent years, however, the range of geophysical information available to potential model makers has greatly increased, not least through the development of seismic arrays. This has led to several attempts to produce more realistic models. Haddon and Bullen (*Phys. Earth Planet. Interiors*, 2, 35; 1969), for example, tried to update the Bullen-A model using eigenperiod data, although modes were only taken up to 44. Press (*Science*, 165, 174; 1969; and others) generated by computer about 5 million random models which he reduced to a handful of successful models consistent with travel-time, eigenperiod and surface wave phase velocity data, although most of these were not entirely consistent with the group velocity data of both Love and Rayleigh waves. This fault was partly remedied by Kanamori (*Phys. Earth Planet. Interiors*, 2, 259; 1970) who modified one of Press's most successful models, although even in this new model (5.08 M) Rayleigh wave velocities deviated from observation at periods below 150 s. Moreover, a predicted layer of very low density between 221 and 421 km may not be physically reasonable.

Appreciating the importance of group velocity data, Mizutani and Abe (*Phys. Earth Planet. Interiors*, 5, 345; 1972) have now derived a new oceanic Earth model (designated OC-1) using a trial and error technique in conjunction with the equations of state for silicates and oxides, which are potential mantle

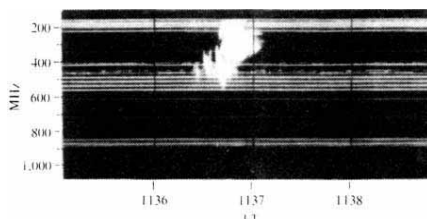
materials. The model has been designed to fit the Earth's total mass and moment of inertia, free oscillation periods for fundamental spheroidal and torsional modes up to 60, Love and Rayleigh wave phase velocities for purely oceanic paths in the period range 100 to 325 s, and Love and Rayleigh wave group velocities for predominantly oceanic paths in the same period range.

The chief characteristics of the model include a pronounced low-velocity layer between 70 km and 210 km (P wave velocity = 7.70 to 7.74 km s⁻¹, S wave velocity = 4.25 km s⁻¹ and density = 3,400 kg m⁻³). Immediately above the low-velocity layer lies a region about 50 to 60 km thick with a high density (3,500 kg m⁻³) and a high S wave velocity (4.72 km s⁻¹). Moreover, between 220 km and 340 km the S wave velocity has a negative gradient (thought to arise from an increase in the iron and pyroxene contents with depth) and there is a suggestion of chemical inhomogeneity with depth in the upper mantle.

The only problems of any significance (and that is debatable) seem to be that the predicted eigenperiods of the torsional mode are systematically higher than the observed ones by about 0.5 s, and the predicted Love wave phase velocities are about 0.01 km s⁻¹ lower than the observed velocities at periods below 200 s. In this the Love waves and torsional modes differ from the Rayleigh waves and spheroidal modes for which prediction and observation agree. Mizutani and Abe note, however, that even these small discrepancies disappear if a small anisotropy of 0.7% is assumed to occur in the low-velocity layer. From the physical point of view, this is not an unreasonable supposition in a low-velocity layer caused by partial melting.

Structure in Solar Radio Bursts

THE solar radio bursts known as type V have been a puzzle since their discovery in 1958. At first, it was thought that their continuum radiation indicated a synchrotron origin, but more detailed observations suggested that Cerenkov radiation from coherent plasma waves is a better explanation, the waves being caused by electrons travelling at about $1/3 c$ which are magnetically trapped in the corona. In that case, harmonic structure ought to be detectable in the type V bursts; in next Monday's



POLLUTION

Atmospheric Oxidation

from a Correspondent

IN a recent issue of the *Journal of the Chemical Society, Faraday Transactions I*, Cox and Penkett report their latest work on oxidation mechanisms in polluted atmospheres (68, 1735; 1972). They have carried out laboratory experiments in which mixtures of SO₂ and ozone are reacted with gaseous olefinic hydrocarbons. On injection of the olefin into the gas mixture the SO₂ is rapidly oxidized to form aerosol particles of sulphuric acid of sub-micron size, with a concomitant drop in the concentration of both ozone and SO₂ (see diagram).

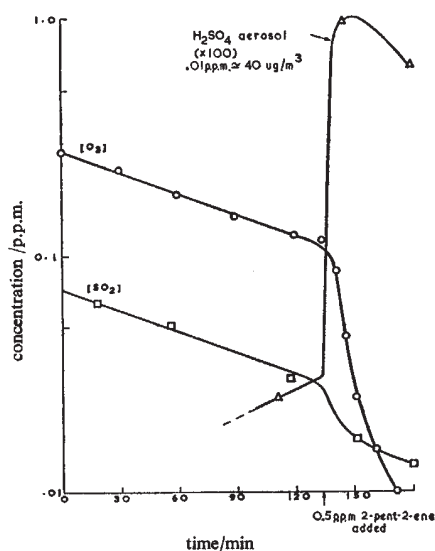
The burning of fossil fuels at present introduces approximately 100 million tons of sulphur dioxide a year into the atmosphere. The fate of the gas after injection has received considerable attention of late, the chief impetus for these studies coming from the realization that increased levels of atmospheric SO₂ might have several harmful effects. These could include increased acidity of rain, and the formation of sulphate aerosols leading to decreased visibility in industrial areas where the input of man-made SO₂ is greatest.

Once in the atmosphere SO₂ may be directly adsorbed onto solid surfaces, taken up by plant leaves or, because of its considerable solubility and reactivity, dissolved in water droplets. Gaseous SO₂ may be oxidized to SO₃ by the action of ultraviolet radiation, atomic oxygen, oxygen or ozone, but such photochemical reactions in the gas phase are probably much less important

Nature Physical Science (March 19) Benz reports the detection of just such a structure.

The observation was associated with a radio flare which began on October 25, 1972. There is no doubt that this was a type V burst, says Benz, and it shows a distinct double structure (see figure). Because the shape of the two humps in the intensity curve is the same, and because two unrelated type V bursts are most unlikely to occur together in this way, it seems that this burst shows harmonic structure with a frequency ratio of 2 to 3.

If type V radiation is preferentially excited in a second harmonic, as has been suggested, the latest observations presumably include second and third harmonics—third order emission from the Sun has previously been found only in one U burst. What the theoreticians will make of this observation remains to be seen.



Curves of concentration against time for the reaction of ozone and SO_2 , showing formation of H_2SO_4 aerosol on the addition of cis-pent-2-ene. (From Cox and Penkett, *J. Chem. Soc., Faraday Trans. 1*, **68**, 1735; 1972.)

in the lower atmosphere than oxidation of dissolved SO_2 to sulphuric acid in water droplets. This is especially true if the droplets contain certain trace metals which act as catalysts for the oxidation. The droplets with sulphuric acid in them will subsequently react rapidly with any ammonium or sodium chloride in the air to form an aerosol of sulphate particles.

Because sulphur dioxide does not react directly with olefins, and the oxidation of SO_2 by ozone occurs only at a slow rate, Cox and Penkett conclude that all three components (ozone, olefin and SO_2) are necessary for rapid formation of the sulphuric acid aerosol.

Various olefins containing between four and six carbon atoms were used in the experiments, the rate of reaction being appreciably faster for internally unsaturated olefins (those in which the double bond is not at the end of the molecule). The rate of reaction is dependent on the concentration of both ozone and olefin, which are consumed in roughly equal amounts. Cox and Penkett consider two possible mechanisms for the process, both of which have the initial reaction of ozone and olefin to form an intermediate as the rate-determining step. In one the ozone bridges across the double bond of the olefin to form a ring complex, and in the other the ozone and olefin form a zwitter (or internal) ion. Whichever intermediate is formed it speedily oxidizes the SO_2 to SO_3 and is itself reduced to an aldehyde. Once produced, the SO_3 will rapidly react with water to form sulphuric acid, which subsequently nucleates to form the aerosol. From the laboratory experiments it seems that the rate of aerosol formation decreases with increase in

relative humidity. Cox and Penkett find no obvious explanation for this result, and conclude that its elucidation must await further information about the intermediate formed in the reaction of ozone and olefin and details of the aerosol formation process.

In the final section of their article Cox and Penkett discuss the application of the SO_2 oxidation rates determined in their laboratory experiments to the real atmosphere. Downward mixing of stratospheric ozone, followed by admixture with urban air containing SO_2 and olefins from fossil fuel combustion, is a possible route for sulphate aerosol formation by means of the ozone-olefin reaction. But because of the rather low concentrations of ozone and olefin in this situation (0.03 and 0.005 p.p.m. respectively) the rate of oxidation of SO_2 is only $0.1\% \text{ h}^{-1}$. In polluted air the levels of ozone may be considerably higher because of photochemical formation of the gas *in situ* by reaction between NO_2 and hydrocarbons. In such environments ozone and olefin levels of 0.1 and 0.05 p.p.m. respectively are not uncommon and the rate at which SO_2 is oxidized to sulphate is about $3\% \text{ h}^{-1}$. Thus in polluted air, where significant amounts of SO_2 , olefin and ozone occur, the oxidation of SO_2 by way of a short-lived intermediate of the olefin-ozone reaction may well be important.

STRESS ANALYSIS

Progress with Lasers

from a Correspondent

AN interesting meeting on holography and laser applications in the analysis of displacement and strain was held at the National Physical Laboratory on February 7. There were nine speakers representing between them the National Engineering Laboratory, the National Physical Laboratory, University College, Swansea, Loughborough University of Technology and the Atomic Weapons Research Establishment (AWRE). It was very clear that the strongest interests represented were those of optics, and that the analysis of strain measurement by these methods still has some way to go. The challenge of most of the work discussed is to make it positively useful in real circumstances, but there were few examples of actual measurements of strain. Of the real applications mentioned, an important subdivision could be drawn between those optical techniques which are an alternative to existing methods and those which enable additional information to be obtained. It is the latter type which is most likely to make an impact on technological developments.

Dr J. M. Burch (NPL) was at pains to point out that holographic interferometry was invented simultaneously by several

Salic Bias of Continental Crust

WHY is it that continental alkaline provinces contain a far higher proportion of salic rocks than do corresponding oceanic areas? For example, up to half the volume of lava in a continental province may comprise rhyolites, phonolites and trachytes, whereas an oceanic island contains very little salic material. Moreover, why is it that in continental provinces salic intrusions are most frequently of central form whereas mafic intrusions are most frequently of dyke form?

In next Monday's *Nature Physical Science* (March 19), Gill proposes a hypothesis which gives plausible answers to both of these questions and which overcomes the principal objection to existing explanations (partial melting and magma stratification) for the salic bias of continents, namely, that such explanations do not actually differentiate between continents and oceans. In other words, although partial melting and magma stratification could lead to the presence of salic material in the continental crust, there is no obvious reason why oceanic crust should be excluded from the action of such processes.

Gill's new hypothesis stems basically from the expected disparity in the time

scales of crustal and mantle processes. The point here is that mafic dyking in alkaline provinces is clearly an intermittent process dependent upon crustal conditions, whereas there is no obvious reason why magma generation should cease just because and when crustal conditions are not appropriate to dyking. It is therefore logical to ask what happens to newly generated magma during periods of no dyking when access to the surface by way of fissures is not possible.

Density considerations suggest to Gill that when continental crust is not amenable to dyking, magma is at first restricted to depths greater than about 10 km where it cools, in time giving low-temperature residual liquids. Because of a relative lack of buoyancy, mafic components of the magma will be confined to this reservoir but the salic magma may rise by stoping and thus give upper crustal central forms. By contrast, oceanic crust offers much less restriction on dyking and so activity is predominantly basaltic. The critical difference between continental and oceanic crust, which leads to the salic bias of the former, is thus simply the different propensities to allow crustal extension.

workers and that both British scientists and American scientists can share that achievement. Perhaps the focal point for laser applications in engineering came with the international meeting in 1968 at the University of Strathclyde, where the engineering applications of holography formed the principal theme. At that time holography had been very widely applied to practically all types of engineering measurement. Some of these applications proved to be successful and work continued, but others fell by the wayside and it was somewhat disappointing on reflexion to see how little progress has been made in the applications field.

One of the chief things required of holography is information about how and why an object moves or how a displacement takes place. Such information is provided in terms of an interference fringe pattern, the interpretation of which has been the subject of much discussion in the past. The topic was again raised at this meeting and it now seems that adequate analysis and solutions are available; this should encourage would-be users to take courage and obtain a laser. The Loughborough group has taken a slightly different line in avoiding the analysis of complex interference patterns by changing the experimental technique to one which effectively uses the interference fringes as a linear scale. Apparatus for doing this was described and results shown from a video tape. The equipment itself is called the Electronic Speckle Pattern Interferometer (ESPI) and it was demonstrated by application to vibration visualization and to dynamic strain visualization in carbon fibre-reinforced plastics.

One application of holographic interferometry in which quantitative analysis of interferograms is not required is non-destructive testing (NDT). Some examples of this were provided by the National Engineering Laboratory where minute cracks are being detected in high-pressure gas cylinders. There is some difference of opinion as to whether the terms non-destructive testing or non-destructive evaluation should be used, but the issue is further complicated by experimental work at the National Physical Laboratory. Here they have shown by means of holographic interferometry that one's eyes bulge on being hit on the head with a hammer. (Safety helmets were worn for these experiments.) Other NDT applications mentioned include the testing of fabricated components for aircraft work and other sophisticated or high reliability applications. The Loughborough ESPI can also be used for such tasks.

Speckle pattern methods came in for considerable discussion involving the NPL and University College, Swansea,

in addition to ESPI. Although it is in many ways similar to holography, speckle pattern interferometry offers a greater degree of sensitivity control. Mr A. E. Ennos (NPL) has used this to desensitize a method of displacement measurement, and Mr A. R. Luxmoore (University College, Swansea) extended discussion on this theme. The apparatus for speckle pattern interferometry can be very simple when photographic recording is used. The work described used an ordinary 35 mm film camera and was stated to give minimal demands on laser coherence. In the case of photographic recording, results are often enhanced by a stage of optical filtering

following the test; very clear fringes are observed under these circumstances. If, however, rapid or on-line results are required there is only marginal advantage over holography.

The meeting was brought back to thoughts on holography by Mr M. R. Wall (AWRE) who shares a place with the early inventors of holographic interferometry. In many ways he set out to explode the myth that holography is for the specialist laboratory only, because in a few moments he explained how, with a pulsed laser, it is possible to record a holographic interferogram of a hot pressure vessel on site and also how to interpret fringes.

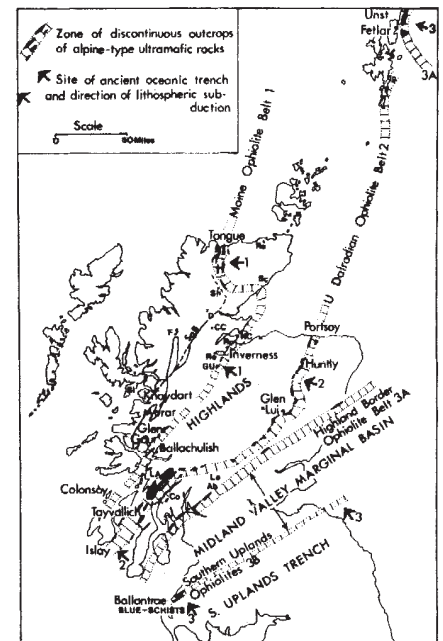
Plate Tectonics in Scotland

IN next Monday's *Nature Physical Science* (March 19), Garson and Plant offer a plate tectonic interpretation of the Scottish ophiolite sequences which is significantly different from that recently given by Dewey (*Scott. J. Geol.*, 7, 219; 1971). According to Dewey, the whole Caledonian orogeny was related to a consuming plate margin to the north of the Southern Uplands, with a northward-dipping Benioff zone along the Southern Uplands fault active between the Lower Ordovician and the Lower Devonian. But as Garson and Plant point out, there are several objections to this interpretation, the most general one being that the Southern Uplands fault seems to be too far removed to explain the ophiolite sequences in the Highlands to the north.

Garson and Plant thus propose a different pattern of development in which the Scottish Highlands mountain belt evolved in three principal episodes corresponding to the three "significant" belts of Alpine-type ultramafic rocks—the Moine, Dalradian and Highland Border Belts (see map), respectively. Thus, whereas Dewey's model envisages a long, passive sedimentation phase followed by a relatively short orogeny, Garson and Plant suggest progressive deformation and addition of continental material with an episodic movement of a consuming plate margin towards the south-east.

In the first of the proposed episodes (Morarian), the Alpine-type ultramafic rocks of the Moine belt were intruded into a eugeosynclinal sequence during a phase of mountain building in the Precambrian (750 to 800 million years ago). Garson and Plant suggest this to have been related to an oceanic plate underthrusting the continental margin at a time when the proto-Atlantic Ocean was closing. The second orogenic episode (Upper Dalradian), which began after the Morarian plate descent had stopped, took place at the edge of a new continental crust extended from its pre-

vious position by the addition of eugeosynclinal and miogeosynclinal sediments from the Morarian episode. At this stage (Lower to Upper Cambrian), the second ophiolite belt was intruded as a new phase of lithospheric descent took place, possibly indicating another closing of the proto-Atlantic Ocean.



The third episode apparently continued the orogenic processes represented by the other two, leading to the emplacement of the Highland Border ophiolite belt during the lower Ordovician, although it is difficult to visualize in detail because of obscuration of the evidence by subsequent faulting and erosion. This only leaves the ophiolites of the Southern Uplands to be accounted for. According to Garson and Plant, the Midland Valley is symmetrical in that the two ophiolite belts which border it are of comparable age. They thus envisage that the Midland Valley originated as a marginal sea.

Linkage Analysis in Man by Somatic Cell Genetics

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Techniques for the study of somatic cell genetics, and particularly those involving the expression of enzyme markers in hybrid cells, have already made possible a large number of gene-chromosome assignments. Genetic and family studies, as well as cellular studies on recombination and gene transfer, promise more and quicker results in the future.

SOMATIC cell hybridization, first demonstrated by Barski *et al.*¹, was an important early step in the formulation of somatic cell genetic systems, allowing as it does the combination of genetically different genomes within a single cell. In a series of investigations Ephrussi and his colleagues showed that hybrid combinations could be obtained between the cells of different species², and that chromosomes of one or both parental genomes could be lost or segregated from the hybrid cell³. Weiss and Green⁴ first demonstrated the practical application of somatic fusion-segregation systems for the purpose of gene mapping in man (see below). Other investigators have contributed useful procedures which enhance the formation of hybrid cells and their enrichment. These developments now allow a completely new cell culture approach to gene mapping in man.

Cultivation of Hybrid Cells

For the formation of hybrid cells the parental cells are mixed together and co-cultivated. Membrane fusion can be enhanced by treatment with inactivated Sendai virus^{5,6} or with lysolecithin⁷. Fusion between two parental cells of different origins gives rise to a binucleate heterokaryon. Heterokaryons have a short life expectancy, and following their first mitosis, generally form mononucleated or hybrid daughter cells which contain chromosomes from both parental genomes. In many parental cell combinations, the hybrids have an infinite life expectancy and can be grown into large clonal cell populations. In man-mouse and man-Chinese hamster hybrids there is a unilateral loss or segregation of human chromosomes. The segregation of human chromosomes is variable in extent in different clones, and in many instances clones can be obtained which maintain for many generations a partial human chromosome constitution. Thus, it is possible in effect to sample different numbers and combinations of human chromosomes in a series of man-rodent hybrids of independent origin. Each clone represents a partial human karyotype superimposed on an intact mouse or Chinese hamster genome. The experimental isolation of partial human chromosome complements forms the basis of somatic cell linkage analysis.

Enzyme complementation has been used to enrich for

hybrids in mixed populations of parental cells. Littlefield has shown that drug resistance mutant cell lines can be useful in this regard⁸. Mutant cell lines can be selected which are deficient in the enzymes hypoxanthine-guanine phosphoribosyltransferase (HGPRT) and thymidine kinase (TK) by exposing cells to the antimetabolites thioguanine and BUdR respectively. HGPRT deficient cells cannot incorporate hypoxanthine, whereas TK deficient cells cannot metabolize thymidine. If *de novo* synthesis of purines and pyrimidines is blocked by the antimetabolite aminopterin, cells become dependent for survival on exogenous hypoxanthine and thymidine. HGPRT and TK deficient cells are thus conditional lethal mutants which are killed by aminopterin irrespective of the availability of hypoxanthine and thymidine. The fusion of HGPRT deficient with TK deficient parental cells yields hybrid cells whose enzyme deficiencies are complemented and which can grow in nonpermissive selection medium containing hypoxanthine, aminopterin, and thymidine (HAT medium). Kusano *et al.* have shown that adenine phosphoribosyltransferase (APRT) deficiency mutations can be used similarly for hybrid cell selection⁹. Conditional lethal mutants other than those based on drug resistance can also be used for hybrid selection. Puck *et al.* have used nutritional auxotrophs with good results^{10,11}, and it is likely that temperature sensitive mutations can be used in the same way¹². Moreover, it is possible to make use of conditional mutant established rodent cell lines in combination with diploid human fibroblasts or leucocytes which have low growth potentials *in vitro*^{12,13}. One can select against the rodent parent using nonpermissive medium and against the human diploid parent by virtue of its inherently poor growth characteristics.

Conditional lethal cell mutants in rodent cell populations are extremely useful for genetic analysis. In nonpermissive conditions only hybrids which retain the complementing human gene will survive. Thus, if one forms hybrids between HGPRT deficient rodent cells and wild type human cells (HGPRT⁺), and cultivates them in HAT medium, only those cells which retain the human HGPRT gene will survive. Generally, the intact human X chromosome which carries the HGPRT gene is retained in the complemented hybrid. It is possible to conceive of a series of rodent cell lines each of which carry different conditional lethal mutations which are complemented by genes on each of the human autosomes and sex chromosomes. Such a panel of rodent cell lines would be extremely useful in mapping studies because each would produce hybrids in which the segregation of a specific human chromosome would be fixed. Conditional lethal mutants of this type are tabulated in Table 1. It should be pointed out that the drug resistance complementation systems also lend themselves to counter selection. Cells which retain TK, APRT, and HGPRT activity are susceptible to the antimetabolites BUdR, fluoro-adenine, and thioguanine, respectively⁸⁻¹⁰. Thus it is possible to use these agents in permissive medium to select against hybrid cells which have retained human chromosomes 17, 16 and X.

Table 1 Conditional Drug Resistance and Nutritional Auxotrophic Genetic Markers

Rodent mutation	Rodent parent	Complementing human enzyme	Human linkage unit
HGPRT deficiency	Mouse	HGPRT ⁺	X
TK deficiency	Mouse	TK ⁺	17
APRT deficiency	Mouse	APRT ⁺	16
Glycine A auxotroph	Chinese hamster	Serine hydroxymethylase	12
Adenine B auxotroph	Chinese hamster	Unknown	4 or 5

Rodent-Human Hybrids

In rodent-human hybrids, the human chromosomes are unilaterally segregated, both homologous human and rodent enzymes are expressed and can be identified, and human and mouse chromosomes can be discriminated and accurately identified on an individual basis. These hybrids are therefore particularly suitable for human gene linkage analysis.

The loss of human chromosomes from mouse-human and Chinese hamster-human hybrids is well documented, but the mechanism of loss is poorly understood. Preferential loss of human chromosomes in rodent X human hybrids, irrespective of the origins of the parental cell populations, is the rule, and only one possible exception has been reported¹⁵. A mechanism of loss suggested by Handmaker (personal communication) is that human chromosomes cannot attach efficiently to the hybrid spindle apparatus and thus have higher incidence of loss. Another possibility, which is not necessarily incompatible with this, is a mechanism of segregation based on random non-disjunction of mouse and human chromosomes in combination with the preferential selection of hybrids which possess partial human karyotypes¹⁶. Nabholz *et al.*¹⁷ have suggested that chromosomes are lost by two temporarily distinct processes. Early loss, possibly during the first several mitotic divisions after fusion, can result in the abrupt loss of a few or many human chromosomes. Late loss is characterized by slow progressive loss in some instances over many cell generations. Nabholz *et al.*¹⁷ have also presented evidence that human chromosomes are segregated non-randomly into hybrid clones. Preliminary results in our laboratory, based on twenty-eight independent hybrid clones, indicate a very low frequency of retention of human chromosome 9 (7%) compared with the overall frequency of human chromosome retention (29%). It has been reported that hybrids with two rodent genomes (2s hybrids) retain more human chromosomes than 1s hybrids¹⁵. The relationship between rodent and human chromosome number is significant and should be resolved, because it is fundamental to the problem of chromosome segregation.

The amino-acid constitution of homologous enzymes between man and rodents generally differs to some degree as a result of evolutionary divergence, and it is generally possible to detect these differences by electrophoretic procedures. There is thus a very large potential catalogue of genetic markers in the rodent-human cell hybrid system, limited only by the development of adequate test procedures. A compilation of isozyme procedures has been reported by Ruddle and Nichols¹⁸.

It is important for genetic testing that the enzyme markers be constitutive—that is, they must invariably be expressed if the corresponding structural gene is retained in the hybrid. Facultative markers are defined as those markers which are subject to modulation and which may not be expressed even if the corresponding cistron is present. It is very

difficult to define phenotypes as being absolutely constitutive or facultative. Generally speaking, enzymes which are expressed in all cell types *in vivo* and which contribute to vital metabolic pathways are termed constitutive, whereas enzymes which are restricted to one or a few specialized cell types and which do not participate in vital metabolic activities at a cellular level are termed facultative. Good evidence exists for the modulation of certain facultative functions in hybrid combinations between parental cells of different epigenetic types¹⁹. This necessarily complicates the linkage analysis of such phenotypes. Phenotypes classified as constitutive may under certain conditions be modulated. For example, hybrid clones have been recovered by Ricciuti²⁰ which possess normal C-7 human chromosomes, but which do not express detectable levels of mannose-phosphate isomerase (MPI) activity. Linkage analysis in other cell hybrids shows a strong correlation between C-7 and MPI. I have concluded that MPI may represent a partially constitutive phenotype. Such phenotypes pose problems for linkage analysis, but they also provide useful material for studies on phenotype modulation.

Cytological Identification of Chromosomes

It is now possible to identify all of the chromosomes of the Chinese hamster, laboratory mouse, and man by cytological procedures. Caspersson and co-workers²¹ have shown that quinacrine binds differentially to specific regions of the human chromosomes, and that each chromosome possesses a unique banding pattern. Mouse chromosomes are similarly unique and the banding patterns have now been correlated with known murine linkage groups²². Giemsa banding procedures provide results comparable with those of quinacrine²³. Pardue and Gall have introduced an *in situ* annealing technique which makes possible the localization of highly redundant DNA in mouse and human chromosomes²⁴. Purified isotopically labelled redundant DNA is annealed to intact chromosomes which have been pretreated with DNA denaturation agents. The labelled redundant DNA is hybridized to complementary DNA in the chromosome, and its location revealed by autoradiography. Pardue and Gall have shown that the murine redundant DNA (satellite DNA) is restricted to the centromere regions and that denaturation followed by Giemsa staining reveals positively staining, constitutive heterochromatin regions in the chromosomes. Arrighi and Hsu²⁵ have adapted this method to the analysis of human chromosomes and subsequent studies have shown a correspondence between constitutive heterochromatin and redundant DNA²⁶. Human and mouse satellite DNA are specific and do not cross react. It is thus possible by hybridization *in situ* to distinguish human and mouse centromeric regions, which has proved useful in the detection of human-mouse chromosome translocations²⁷ (see below). Several laboratories have reported evidence indicating that the centromeric constitutive heterochromatin in man has different physical properties unique for several of the human chromosomes²⁸.

Assigning Genes to Chromosomes

Linkage of enzyme phenotypes can be inferred from their concordant segregation. The human chromosomes maintain their integrity for the most part, seldom undergoing rearrangement or deletion, and the concordant segregation of markers thus provides evidence for their location on the same chromosome irrespective of map distance. It is therefore appropriate to employ the term "synteny" coined by Renwick to signify merely localization on the same chromosome. Synteny testing is performed by comparing the segregation pattern of all markers in all pairwise combinations. The synteny test is less biased if performed on

clones of independent origin and the detection of valid syntenic relationships is enhanced by using clones derived from separate hybridization experiments, using different hybrid combinations. This generally entails computer analysis because of the number of clones and markers involved.

Individual genes or syntenic genes can be assigned to specific chromosomes by tabulating the human chromosomes in each of the clones and correlating them with the enzyme markers. The concordant presence or absence between a chromosome and a phenotype provides evidence for the assignment of the gene governing a particular phenotype to a specific chromosome. Twenty to thirty metaphases are analysed per clone by means of quinacrine banding, Giemsa banding, or constitutive heterochromatin staining techniques. Identification is enhanced if cells are first photographed by quinacrine fluorescence and then by constitutive heterochromatin staining procedures.

It is frequently possible to strengthen the assignment of a gene to a particular chromosome by correlating the frequency of a particular chromosome within a clone with the intensity of expression of an assigned phenotype(s). Discrepant clones of two classes can occur, however. In the first, presuming a valid assignment, the chromosome cannot be detected but the phenotype is present. We have demonstrated cryptic, rearranged chromosomes in a number of such instances which explain an apparently discordant chromosome/gene relationship²⁹. A second type of discrepant clone involves the presence of a specific chromosome, but the absence of its corresponding phenotype(s). Clones of this type are difficult to explain, but could involve subtle rearrangements in chromosome structure, gene mutation, modulation of gene expression, or technical failure in phenotype detection.

It is possible to assign genes to particular regions of chromosomes such as chromosome arms, or band regions as defined by particular staining reactions. This can be accomplished by making use of chromosome rearrangements such as translocations and deletions in the human parental cell population or by making use of spontaneous chromosome rearrangements which are generated in the hybrids. Translocations of chromosomes to or between chromosomes X, 17, and 16 are useful because these chromosomes possess selectable loci. A number of translocations affecting the same chromosome but with different break-points can be used to restrict the localization of genes. For this purpose it will be particularly useful to characterize and store in central repositories all detected human translocations, to serve as a library of rearrangement products for future somatic cell gene mapping. Programs of human mutant cell banking are now being formulated in several countries. An example of regional linkage assignments based on translocations in parental cells is cited below for the X chromosome.

It is also possible to make use of spontaneous, sporadic chromosome rearrangements which occur in hybrid cells to fix the location of genes within subregions of particular chromosomes. Human chromosomes within hybrids may undergo rearrangement and even translocation to mouse chromosomes²⁹ and it has been possible to make use of such rearrangements to restrict the localization of the thymidine kinase gene to the long arm of human chromosome 17²⁹. The translocation of human chromosome segments to the mouse chromosome set is significant from a genetic point of view because it may serve to restrict the further segregation of human genes involved in the translocation. It is conceivable that treatment of parental cells or hybrids with physical or chemical chromosome breaking agents could be used to induce chromosome rearrangements. Enrichment procedures could be devised to select particular classes of rearrangement products. Such systems could be used to increase the resolution of subregional chromosome gene assignments.

Known Human Linkage Groups

A significant number of syntenic relationships and chromosome assignments has been established by somatic cell genetics. A survey of the current linkage information is presented below for each of the human chromosomes in turn. The results are also summarized in Table 2. For chromosome 1, Van Cong *et al.*³⁰ have reported a syntenic relationship between phosphoglucomutase-1 (PGM₁) and peptidase C (Pep C) using mouse-human hybrids. This syntenicity has been confirmed by Ruddle *et al.*³¹. Using Chinese hamster-human hybrids, Westerveld *et al.*³² have reported a syntenicity between 6-phosphogluconate dehydrogenase (PGD) and Pep C. Taken together, these findings imply that PGD, Pep C, and PGM₁ are all syntenic. Pep C has been assigned to chromosome 1 using mouse-human cell hybrids³¹. This assignment has been confirmed by the assignment of PGD to chromosome 1 independently by Bootsma *et al.* (personal communication) and Hamerton *et al.*³⁴ using Chinese hamster-human hybrids. If the findings based on cell hybrids are combined with linkages known from human pedigree analysis, the following additional gene markers can be assigned to chromosome 1: zonular pulverulent cataract, Duffy blood group, auriculo-osteodysplasia, salivary amylase, pancreatic amylase, elliptocytosis and rhesus blood group. For complete literature citations see Ruddle *et al.*³¹.

Table 2 Assignments of Genes to Chromosomes

Chromosome 1	PGM ₁ , 17190; PGD, 17220; Pep C, 17000
Chromosome 2	IDH, 14770; MOR, 15425
Chromosome 3	—
Chromosome 4-5	Adenine B ⁺ , 10265
Chromosome 6	MOD, 15420; IPO-B, 14745
Chromosome 7	MPI, 15455; PK ₃ , 17905
Chromosome 8-9	—
Chromosome 10	GOT, 13825
Chromosome 11	LDH-A, 15000; Es-A ₄ , 13340; KA, 14875
Chromosome 12	LDH-B, 15010; Pep B, 16990; GlyA ⁺ (serinehydroxymethylase ?), 13845
Chromosome 13	—
Chromosome 14	NP, 16405
Chromosome 15	—
Chromosome 16	APRT, 10260
Chromosome 17	TK, 18830
Chromosome 18	Pep A, 16980
Chromosome 19	GPI, 23575
Chromosome 20	ADA, 10270
Chromosome 21	IPO-A, 14744; AVP, 10745
Chromosome 22	—
Chromosome X	HGPRT, 30800; PGK, 31180; GPD, 30590; α-Gal, 30150
Chromosome Y	—

These genes were assigned or confirmed by cell hybrid analysis. Each trait is identified by McKusick's human gene catalogue number⁵⁹. IPO-A and B used here agree with the original designation of Brewer⁵³.

Preliminary results in our laboratory (R. P. Creagan and F. H. R.) suggest that isocitrate dehydrogenase (IDH) and NADP-malate dehydrogenase (MOD) which have been shown to be syntenic⁴⁴ can be assigned to chromosome 2. No loci have been assigned to chromosome 3. For chromosomes 4 and 5, Kao and Puck³⁵ using Chinese hamster-human

hybrids have demonstrated a positive association between hamster adenine B auxotrophy and a human B group chromosome when hybrids are propagated on minimal medium. The specific enzyme involved is unknown. Chen *et al.*³⁶ using mouse-human hybrids have shown that cytoplasmic malate dehydrogenase (MDH) is assignable to chromosome 6 and there is evidence to support a syntenic relationship between indolephenol oxidase, tetrameric form B (IPO-B) and MDH (J. A. Tischfield, R. P. Creagan and F. H. R., unpublished).

McMorris *et al.*³⁷ using mouse X human hybrids have assigned mannose phosphate isomerase (MPI) to chromosome 7. Shows³⁸ has reported a syntenic relationship between MPI and the leucocytic form of pyruvate kinase, (PK_L).

There are no assignments to chromosomes 8 or 9. There is evidence from mouse-human hybrids for the assignment of the cytoplasmic form of glutamate oxaloacetate transaminase (GOT) to chromosome 10 (unpublished work of R. P. Creagan, J. A. Tischfield, F. A. McMorris, M. Hirschi, T. R. Chen and F. H. R.).

Boone *et al.*³⁹ using mouse-human hybrids have assigned lactate dehydrogenase A (LDH-A) to chromosome 11. Shows³⁹ using mouse-human hybrids has reported a syntenic association between LDH-A and human esterase A₄ (EsA₄). Van Someren *et al.*⁴⁰ have reported a syntenic association between glutamic-pyruvic transaminase (GPT-C) and LDH-A. The possibility exists, however, that their enzyme detection system is recording LDH-A activity. This may also apply to LDH-B and GPT-B (see below). Nabholz *et al.*¹⁷ using mouse-human cells have reported a positive correlation between the segregation of LDH-A or B activity and sensitivity of hybrid cells to anti-human cytotoxic antisera. Puck *et al.*⁴¹ have reported on the segregation of a possibly similar human antigen(s) in Chinese hamster-human hybrid cells, which they have found to be syntenic with LDH-A.

Ruddle and Chen⁴² and Chen *et al.*³⁶ using mouse-human hybrids have demonstrated positive correlation between lactate dehydrogenase B (LDH-B) and chromosome 12. Hamerton *et al.*³⁴ have confirmed this assignment using Chinese hamster-human hybrids. In mouse-human hybrids a syntenic relationship has been demonstrated between LDH-B and peptidase-B (Pep-B)^{14,43}. The Pep-B/LDH-B syntenic has been confirmed by Shows^{39,44}, Van Cong *et al.*³⁰ and van Someren *et al.*, who have also reported a syntenic association between glutamic-pyruvic transaminase-B (GPT-B) and LDH-B⁴⁰. Jones *et al.*⁴⁵ using Chinese hamster-human hybrids have reported a syntenic relationship between LDH-B and the complement to the Chinese hamster glycine auxotrophic mutant A. Serine hydroxymethylase has been implicated as the specific deficiency in glycine A auxotrophy.

No assignments have been made to chromosome 13. For chromosome 14, Ricciuti and Ruddle (ref. 46 and F. Ricciuti and F. H. R., unpublished) using a 14/X translocation in a human diploid fibroblastic cell strain (KOP) hybridized to a mouse cell line have demonstrated a segregation of nucleoside phosphorylase (NP) with the X linked markers, HGPRT, GPD, and PGK. Somatic cell genetic⁴⁶ and family studies⁴⁷ have provided evidence for the autosomal linkage of NP. The studies of Ricciuti and Ruddle thereby support the assignment of NP to chromosome 14. Unreported experiments from our laboratory using a 14/22 translocation also confirm the assignment of NP to chromosome 14. Hamerton *et al.*³⁴ have reported results based on Chinese hamster-mouse hybrids which are consistent with the above findings of Ricciuti and Ruddle. No assignments have been made to chromosome 15.

Tischfield and Ruddle (unpublished) using an adenine phosphoribosyltransferase (APRT) deficient mouse cell line hybridized to normal human diploid cells have obtained evidence for the assignment of APRT to chromosome 16.

On evidence from family studies, Robson *et al.*⁴⁸ have assigned α -haptoglobin to chromosome 16. APRT activity variants have been reported in man, and it would be reasonable to identify kindreds in which α -haptoglobin and APRT variants are jointly expressed to test for linkage between these two markers.

For chromosome 17, Green⁴⁹ and Migeon and Miller⁵⁰ using mouse-human cell hybrids assigned thymidine kinase (TK) to an E group chromosome. This assignment was based on the earlier findings of Weiss and Green⁴ and has since been verified by Boone and Ruddle⁵¹. Miller *et al.*⁵², Ruddle and Chen⁵³, and Boone *et al.*²⁹ have now assigned TK specifically to chromosome 17. Boone *et al.*²⁹, making use of a spontaneously occurring 17 translocation to a mouse chromosome, have provided evidence for the assignment of TK to the long arm of chromosome 17. Kit *et al.*⁵⁴ and McDougall *et al.*⁵⁵ have demonstrated that adenovirus 12 infection induces host TK activity, and concurrently a secondary constriction in the proximal segment of the long arm of 17. These findings suggest that the TK gene may be located near the adeno-12 induced gap region.

Creagan *et al.* (unpublished) using mouse-human cell hybrids have provided evidence for the assignment of peptidase-A (Pep-A) to chromosome 18.

Glucosephosphate isomerase (GPI) has been assigned to chromosome 19 on the basis of evidence from mouse-human cell hybrids³⁷. Hamerton *et al.*³⁴ have confirmed this assignment using Chinese hamster-human cell hybrids. Linkage studies in the mouse have revealed a loose linkage between GPI and β haemoglobin: it will be of interest to test for a similar linkage relationship in human kindreds.

Boone *et al.*²⁹ using mouse-human hybrids reported a weak association between cytoplasmic isocitrate dehydrogenase (IDH), cytoplasmic maleate oxidoreductase (MOR) and chromosome 20. More extensive data from mouse-human hybrids have now shown that IDH and MOR cannot be assigned to 20 and using mouse-human hybrids we have obtained evidence of the assignment of tissue-specific adenosine deaminase (ADA) to chromosome 20 (J. A. Tischfield, R. P. Creagan and F. H. R., unpublished). ADA is asyntenic with both IDH and MOR. Family studies have demonstrated linkage between HL-A phosphoglucomutase 3, P blood group, and ADA⁵⁶.

On chromosome 21, Tan *et al.*⁵⁷, using somatic cell hybrids, have provided evidence for the syntenic association between indolephenoloxidase-A, dimeric (IPO-A) and a genetic factor (AVP) which controls an antiviral response specifically induced by human interferon. The genetic factor may regulate the interferon receptor and/or the antiviral protein. We have also shown that the interferon and AVP loci are asyntenic⁵⁷. These results confirm earlier studies by Cassingena *et al.*⁵⁸ on their asyntenic association based on monkey-rat somatic cell hybrids. Tan *et al.*⁵⁷ have assigned AVP/IPO-A to chromosome 21. No assignments have yet been made to chromosome 22.

Glucose-6-phosphate dehydrogenase (GPD), hypoxanthine-guanine phosphoribosyltransferase (HGPRT), and phosphoglycerate kinase (PGK) have all been assigned to the X chromosome by segregation analysis in families⁵⁹. Nabholz *et al.*¹⁷ using mouse-human hybrids confirmed the X linkage of HGPRT. Meera Kahn *et al.*⁶⁰ have demonstrated the X linkage of PGK by cell hybrid analysis. Ruddle *et al.*⁶¹ using mouse-human hybrids confirmed the X linkage of HGPRT, glucose-6-phosphate dehydrogenase (GPD), and phosphoglycerate kinase (PGK). Grzeschik *et al.*⁶² have recently provided evidence based on Chinese hamster-human hybrids for the assignment of α -galactosidase (α -Gal) to the X chromosome. In an earlier report, Grzeschik *et al.*⁶³ analysed cell hybrids between human KOP cells which possess a 14/X translocation (KOP) and mouse and Syrian hamster cells. They observed an infrequent segregation of HGPRT and GPD from PGK, which led

them to postulate the assignment of PGK to the long arm, and the possible assignment of HGPRT and GPD to the short arm, although assignment to the long arm was not altogether discounted. Ricciuti and Ruddle (ref. 46 and unpublished results) using the same KOP material hybridized to mouse cells have obtained data which indicate that all three markers are located on the X long arm. This suggests that PGK is proximal to the centromere and distant from the other two markers. HGPRT and GPD seem to be close together and distal to the centromere with respect to PGK; preliminary evidence indicates that HGPRT is proximal to GPD. P. Gerald and co-workers (personal communication) have recently studied a human cell with a 19/X translocation hybridized to mouse cells. A translocation product composed of the 19 long arm, the proximal half of 19 short arm, and the distal half of the X long arm was correlated with GPI, HGPRT, and GPD, but not PGK. This result is consistent with the human X linkage map proposed by Ricciuti and Ruddle⁴⁶. It also confirms the assignment of GPI to 19.

No assignments have been made to the Y chromosome.

Possibilities for New Approaches

The development of a detailed human genetic map is certain to provide insight into the evolutionary origins of man and the primates. LDH-A and LDH-B are located on chromosomes 11 and 12 respectively. These chromosomes are similar in size, centromere position, and banding pattern, which is consistent with the occurrence of a primordial polyploid event in the early primate genome as discussed by Comings⁶⁴. Somatic cell genetic analysis should be feasible for representative members of the order primates using rodent-primate hybrids. Linkage data from such hybrids should provide information on the relatedness of these forms, and yield estimates for rates of evolutionary divergence, especially when combined with comparative studies on the chromosome constitutions and amino-acid sequences of proteins in the representative specimens.

It is already obvious that somatic cell genetics has contributed and will in the future contribute important data to human genetics. Moreover, these developments enhance the significance and future role of family and population genetic studies. Already map distances between genes have been refined or established by the certain knowledge from somatic cell genetics that certain gene pairs are syntenic. We should expect a fruitful interaction and collaboration between practitioners of somatic cell genetics and classical genetics. We must, however, keep clearly in mind that somatic genetic procedures as they now exist are still unacceptably slow and linkage estimates cannot yet be made. If we are soon to develop genetic maps of man comparable to those available for the lower eukaryotes, it will be necessary to develop new procedures. Possibilities for this are to be found in somatic cell recombination and gene transfer.

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Further Evidence of Lower Pleistocene Hominids from East Rudolf, North Kenya, 1972

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Thirty-eight fossil hominids were collected during the 1972 season at East Rudolf, and the total now known from this locality is eighty-seven. Several specimens, including some attributable to *Homo*, were recovered from deposits that are below the KBS Tuff dated at 2.61 million years.

THIS report summarizes the results of the continuation of work carried out during 1972 at East Rudolf. Preliminary reports for the years 1968–1971 have already been published^{1–3}.

A further thirty-eight fossil hominids were collected during 1972, bringing the total now known from this locality to eighty-seven. The collection includes cranial and postcranial material. Several specimens were recovered from deposits that are below the KBS Tuff (2.61 m.y.⁴); these are of particular interest in view of the presence of at least two distinct forms of hominid at this early period. In this report, as before^{1–3}, I have avoided specific identifications and have made provisional attributions to either *Australopithecus* or *Homo*. I believe that the final analysis of the hominids from East Rudolf should be based on as large a sample as can be reasonably available, and there is every indication that further material will be recovered with the continued investigation of the area.

The palaeontological investigations were directed by Dr J. M. Harris (Kenya National Museums), and further specimens of several taxa were collected. Some specimens collected from below the KBS Tuff should prove of considerable interest and value regarding the interpretation of the lower Pleistocene genera⁵. With the extension of exploration at East Rudolf, a unified system of locality numbers designating collecting areas has been devised by Dr V. Maglio who has provided an area map and a simplified diagrammatic representation of correlations between the principal areas⁵.

Archaeological exploration and excavations were continued under the supervision of Professor Glynn Isaac (University of California, Berkeley), assisted by graduate students. The excavations within the KBS Tuff⁶ were extended and a series of sites above the KBS Tuff were examined; a large collection of artefacts was recovered from several preliminary excavations. A detailed report on the archaeological activities will be presented elsewhere.

Mr Bruce Bowen (Iowa State University) extended the geological survey and mapping south of the Koobi Fora ridge

and has established the broad continuity of the sequence from the lowest deposits at Kubi Algi, about 4.5 m.y., to the uppermost deposits at Ileret, about 1.0 m.y.

Mr Ian Findlater (Birkbeck College, London) continued the field investigation and mapping of volcanic events, and Drs J. Miller and F. Fitch are dating the volcanic horizons. In spite of meticulous collecting and rigorous laboratory analysis, however, dates for the tuffaceous horizons above the KBS Tuff continue to prove unreliable. Some intriguing technical problems indicate that depositional complications are causing the conventional techniques of radiometric age determinations to give inconclusive results. Thus there has been no advance on the situation as reported by Maglio⁵, although there is no evidence to suggest that the 2.61 ± 0.26 m.y. BP date from the KBS Tuff is unreliable (personal communication from J. A. Miller). The continued palaeomagnetic studies by Dr A. Brock (University of Nairobi) together with faunal correlations further strengthen confidence in this date.



Fig. 1 Occlusal view of juvenile mandible KNM-ER 1477.

In the summary which follows of the 1972 hominid collection a brief mention is made of the more important specimens; detailed descriptions of all the specimens will be given shortly elsewhere. The specimens attributed to *Australopithecus* are

listed in Table 1; the specimens attributed to *Homo* are listed in Table 2; and the specimens which have not yet been attributed to a particular genus, either because they are too fragmentary, or because a more detailed study is first required, are listed in Table 3. These tables also include geographical and stratigraphical data. The stratigraphical correlation of the areas 119, 121, 123, 127 south of the Koobi Fora ridge has yet to be concluded, so, for the present, this information is omitted for specimens from these areas. Specimens 1510 and 1590 to 1593 were discovered after the 1972 expedition had closed its principal research activities; these specimens, although important, are therefore only listed in the tables and not mentioned further. A separate article will be published⁷ giving details of the *Homo* specimens, KNM-ER 1470, 1472, 1475 and 1481, in order to allow adequate treatment of these important finds.

Australopithecine Material

Eighteen individuals, listed in Table 1, were collected. A number of specimens represent associated parts from the same individual. Several finds refer to horizons below the KBS Tuff so that there is now evidence of the species at East Rudolf during a period of more than 1 m.y.

Table 1 1972 Material Attributed to *Australopithecus*

KNM-ER No.	Specimen detail	Area	Stratigraphic position where known
1463	Right femur diaphysis	1A	Below middle tuff
1464	Right talus	6	Below lower tuff
1465	Proximal fragment left femur	8	Below upper tuff
1467	Isolated M ₃	3	Below upper tuff
1468	Right mandible	8	Below middle tuff
1469	Left mandible, M ₃	131	Below KBS Tuff
1471	Proximal half right tibia	131	Below KBS Tuff
1476	Left talus, proximal tibia and fragment tibia shaft	105	At or above KBS Tuff
1477	Juvenile mandible with teeth	105	At or above KBS Tuff
1478	Cranial fragments	105	At or above KBS Tuff
1479	Fragments isolated molars	105	At or above KBS Tuff
1500	Skeletal elements	130	Below KBS Tuff
1503	Proximal right femur	123	—
1504	Distal right humerus	123	—
1505	Proximal fragment left femur and fragment of shaft	123	—
1506	Right mandible, M ₁ , M ₂ and isolated P ⁴ , P ³	—	—
1509	Isolated teeth, P ₄ -M ₃	119	—
1592	Distal half femur	12	Below lower tuff

A left half of a mandible, KNM-ER 1469, provides evidence that the large form of *Australopithecus* had developed before deposition of the KBS Tuff 2.6 m.y. ago. The mandible is cracked, although a large portion of M₃ is preserved *in situ* together with the roots and parts of the crowns of M₂ and M₁.

A mandibular fragment, KNM-ER 1506, includes M₁ and M₂ *in situ* and isolated P³, P⁴; the M₂ shows a distinct wear facet for M₃ but this tooth seems to have been lost before fossilization. The significance of the specimen is its small size; the body demonstrates the high degree of robusticity seen in other australopithecine mandibles from East Rudolf, and, for the first time, teeth of a small individual are preserved and provide crown dimensions.

A juvenile mandible, KNM-ER 1477 (see Fig. 1), discovered by Mr Musa Mbithi, a Kenyan, is beautifully preserved. The following teeth are in place: the left c, the left and right dm₁, dm₂ and erupting M₁. The germs of the left P₃ C, and I₂ were dislodged from their crypts and were recovered separately,



Fig. 2 Anterior views of (from left to right) femur KNM-ER 1503; humerus KNM-ER 1504; and femur KNM-ER 1505.

whereas the corresponding tooth germs on the right side are preserved within their crypts.

Several postcranial specimens were recovered and a significant difference in the size of some of the specimens may provide additional evidence of sexual dimorphism in this group^{2,3}. A specimen, KNM-ER 1500, which was also recovered from deposits below the KBS Tuff, includes parts of an associated skeleton. The specimen—a small individual, probably female—was discovered by a Kenyan, Mr John Kimengech, and it represents the first certain association of upper and lower limb elements of *Australopithecus* from East Africa. Unfortunately the material is badly weathered and considerable detail has been lost. The following skeletal elements have been identified: the proximal portions of the right femur, radius and ulna, and left tibia; the distal portions of the right femur, and fibula and left tibia; and scraps of the shafts of the tibia, ulna and humerus. This specimen should provide important new evidence on limb proportions in addition to morphological details of australopithecine postcranial bones that have not been available before.

A specimen, KNM-ER 1476, provides information on an associated tibia and talus, the former showing features similar to the australopithecine tibia, KNM-ER 741^{2,8}, previously reported. The talus exhibits a marked lateral extension for the articulation of the lateral malleolus which is also seen in a complete talus, KNM-ER 1464. This feature seems to be a characteristic of australopithecine tali and together with a number of other features makes this foot bone quite distinctive of this group.

Three specimens collected from area 123, KNM-ER 1503, 1504 and 1505 (see Fig. 2), probably represent parts of the same individual. The proximal portion of the right femur, KNM-ER 1505, is beautifully preserved and shows the characteristic long neck and small head seen in all other australopithecine femora⁹. The distal fragment of humerus is very similar to the humerus, KNM-ER 739^{2,8}, but it is smaller. It shows the marked extension of the medial epicondyle, the constricted trochlea, and the relatively large capitulum.

Hominine Material

Sixteen individuals, listed in Table 2, are represented by the material collected during 1972. Evidence of *Homo* at levels below the 2.6 m.y. KBS Tuff horizon will be put forward on the basis of some remarkable material that will be discussed in a separate report⁷.

A fragment of parietal, KNM-ER 1466, is notable; it is thick boned and bears a marked temporal ridge, features which are reminiscent of the calvaria from Olduvai Gorge (OH9)¹⁰. The specimen is unfortunately incomplete, and therefore cannot provide any conclusive evidence for the presence of this species at East Rudolf.



Fig. 3 Occlusal view of mandibles (from left to right) KNM-ER 1507, 1502 and 1501.

The mandibular fragments, KNM-ER 1501, 1502 and 1507 (see Fig. 3), from areas south of the Koobi Fora ridge are gracile and show a morphology similar to that seen on the *Homo* mandible from Ileret, KNM-ER 992³.

Material of Unclear Affinities

Among the specimens listed in Table 3 a mandible, KNM-ER 1482 (see Fig. 4), is of particular interest; it shows characters not seen in either the contemporary *Australopithecus* or the assemblage of *Homo* mandibles from East Rudolf. The specimen was recovered from deposits below the KBS Tuff.

Significance of the 1972 Finds

The recovery of *Australopithecus* from levels below the KBS Tuff is particularly important in view of the close similarity of this material to that from the upper part of the East Rudolf succession. A pre-Pleistocene emergence of this genus seems reasonable although no precise data to support this have yet been put forward. Now that a large number of specimens to

Table 3 1972 Material of Unclear Affinities

KNM-ER No.	Specimen detail	Area	Stratigraphic position where known
1473	Proximal fragment of right humerus	131	Below KBS Tuff
1474	Parietal fragment	131	Below KBS Tuff
1482	Mandible, partial dentition	131	Below KBS Tuff
1515	Isolated incisor	103	Below Koobi Fora Tuff

Australopithecus are known from East Africa, the taxonomic attribution of the mandibular specimen, KNM-ER 329 from Lothagam Hill, to *Australopithecus c.f. africanus*¹¹ might be questioned. The evidence for the presence of the "gracile" form of *Australopithecus* in East Africa is limited. The fragmentary nature of this specimen makes specific identification very difficult, particularly in the absence of other material from deposits of an equivalent age; only a few isolated dental fragments from the Usno Formation in the Omo Valley¹² are known. The generic attribution of the Lothagam specimen to *Australopithecus* might be questioned on the grounds that the specimen could equally well represent a Pliocene form such as the East African representative of the genus *Ramapithecus*. Such a conclusion would radically alter the interpretative model of hominid evolution.

The additional postcranial material will provide further evidence on which to examine the significance of the locomotory behaviour of *Australopithecus*. Although there is a growing body of evidence in support of a bipedal model, it is important to recognize that the australopithecine mode of bipedality may have been quite distinctive from that of other contemporary hominids and behaviourally significant. In view of the evidence for contemporary *Homo* with morphologically distinct limb elements, some consideration must be given as to whether the australopithecine pattern of bipedal adaptation really reflects a transitional phase as has been suggested. The associated skeletal material collected during 1972 will advance the study of limb proportions within *Australopithecus*; preliminary indications point to a relatively short lower limb and a longer forelimb.

Table 2 1972 Material Attributed to *Homo*

KNM-ER No.	Specimen detail	Area	Stratigraphic position where known
1462	Isolated M ₃	130	Below KBS Tuff
1466	Parietal fragment	1	Below upper Tuff
1470	Cranium	131	Below KBS Tuff
1472	Right femur	131	Below KBS Tuff
1475	Proximal right femur	131	Below KBS Tuff
1480	Isolated molar	105	Above KBS Tuff
1481	Left femur, proximal tibia, distal tibia and distal fibula	131	Below KBS Tuff
1483	Mandible fragments	131	Below KBS Tuff
1501	Right mandible	123	—
1502	Right mandible with molar	123	—
1507	Juvenile left mandible with teeth	127	—
1508	Isolated molar	127	—
1510	Cranial fragments	119	—
1590	Cranial fragments with juvenile dentition	12	Below KBS Tuff
1591	Humerus lacking head	12	Above KBS Tuff
1593	Cranial and mandibular fragments	12	Below KBS Tuff



Fig. 4 Occlusal view of mandible KNM-ER 1482.

The hominine collection provides further examples of the fragile mandibles previously reported from the Ileret area³. Although the dating for the deposits south of Koobi Fora remains tentative, the fauna associated with these new mandibles indicates that they are earlier than those from Ileret. As such, it is possible to postulate a range of time that is greater than that represented by Ileret and the Olduvai Bed II deposits from which similar material has been reported. Mandibular material for the hominid represented by the cranium, KNM-ER 1470⁷, is not known at present but the size and shape of the palate of this specimen suggest a fairly broad big-toothed mandible, quite unlike the fragile specimens just mentioned. The affinities of the mandible, KNM-ER 1482, found in the same locality as the cranium KNM-ER 1470, are far from clear.

In conclusion, I would like to stress that the 1972 collection of hominids has raised more questions than answers; it now seems clear that the pattern of hominid evolution in eastern Africa is extremely complex. Evidence for local geographical variation in various mammalian taxa, primate and non-primate, is emerging, with significant differences occurring within forms restricted to small geographical zones such as the Omo/East Rudolf basin. Until further data on palaeogeographical barriers, environments and chronology are available the interpretation and the erection of evolutionary models should remain tentative.

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Particle Injection in the Cygnus X-3 Radio Outburst

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Particle injection played an important role in the recent Cygnus X-3 radio outburst. Calculations on the basis of an improved expanding cloud model show that a maximum mass of $0.76 \times 10^{-8} M_{\odot}$ was injected over a period of 1.2 days.

THE mass of data from the recent radio outbursts in Cygnus X-3 provides an excellent opportunity to test ideas on radio variability. Monitored at least at eight frequencies during its entire ten day duration, the first of these outbursts yielded flux density data complete and well-defined enough to allow more precise determination of model parameters than previously possible for events of this kind. Here I examine in detail the first of these outbursts (September 2–11) using the generally accepted adiabatic expansion model modified to incorporate a prolonged injection.

According to the conventional model, the observed flux is synchrotron radiation produced by an adiabatically expanding cloud of relativistic electrons. Initially, the cloud is small and the electron density high enough for re-absorption of the synchrotron radiation to occur; the cloud is opaque to its

own radiation. As the cloud expands, the decreasing electron density results in an increase in the observed flux at a given frequency. The flux density reaches a peak just as the cloud makes the transition from its opaque to its transparent phase where the electron density is low enough for re-absorption to be negligible. At the higher frequencies, the flux density peaks earlier since the more energetic radiation penetrates the cloud more readily. Finally, the flux falls off as the electrons continue to lose energy to the adiabatic expansion. In this formulation of the model, the number of electrons is assumed to be constant throughout source evolution.

This model accounts well for the flux density development during the late part of the outburst¹, but fails by a wide margin to fit the development at the beginning. The problem is highlighted in the discrepancy between the peak flux densities observed at the high frequencies, and the much higher values required by the model. The origin of this discrepancy lies with the model assumption that all electrons are present and radiating in the source from the beginning. According to the model, the source should become quickly transparent at the high frequencies and yield high fluxes before expansion losses significantly reduce electron energy. Only if fewer relativistic electrons are present initially in the source or if some additional suppression mechanism other than self-absorption is at work can the adiabatic expansion model be made to conform with the data.

The simple device of a particle injection of specific duration,

which can be expressed analytically in the model equations, significantly improves the model's description of the Cygnus X-3 outburst. If electrons are introduced gradually into the source so that there are a small number initially producing a correspondingly small flux which builds as the electron number increases, then the observed behaviour of the flux density may be adequately reproduced.

Model Equations

I adopt a rate of particle injection which is constant over a time ζ , after which it falls to zero. It may be represented by the normalized form:

$$dN/dt = (1 + \exp(t - \zeta)/\epsilon)^{-1} \approx \begin{cases} 1; & t < \zeta \\ 0; & t > \zeta \end{cases} \quad (1)$$

N is the total number of electrons injected into the source as a function of time; ϵ is the time scale for the injection rate to fall to zero. For small ϵ , the rate is simply a step function. This is not the only allowed form for the injection rate. Its simplicity and previous success at interpreting similar outbursts in extragalactic radio sources² recommend its further application here.

The flux density observed from a self-absorbed spherical cloud composed of synchrotron radiating electrons isotropic in velocity and uniform in spatial distribution is^{3,4}

$$S_\nu = \pi a_\gamma (3.18 \times 10^{-31}) r^2 R^{-2} H^{-1/2} \nu^{2.5} [1 - e^{-\tau}] \quad (2a)$$

$$\tau = 2b_\gamma (0.019) (3.5 \times 10^9)^\gamma r K H^{(\gamma+2)/2} \nu^{-(\gamma+4)/2} \quad (2b)$$

where τ is the source opacity. The frequency of observed radiation ν , the magnetic field strength in the source H , the distance, R , to the source, and its radius r , must be given in c.g.s. units. The coefficients a_γ and b_γ are known, slowly varying functions of γ of order unity. The factors π and 2 derive from the geometry of the source. K and γ occur in the electron differential energy distribution, which is assumed to be a power law:

$$n(E, t) dE = K E^{-\gamma} dE \quad (3)$$

n represents the number of electrons per unit volume in the energy interval E to $E + dE$. From equations (1) and (3) with the fundamental assumption that the electrons lose energy as r^{-1} to the adiabatic expansion, it follows that K must have the form:

$$K = k(r/r_0)^{-2-\gamma} f(t) \quad (4a)$$

$$f(t) = \epsilon \ln(1 + \exp(\zeta/\epsilon)) (1 + \exp(-(t - \zeta)/\epsilon))^{-1} \approx \begin{cases} \zeta; & t < \zeta \\ 1; & t > \zeta \end{cases} \quad (4b)$$

where k is a constant, and r_0 is the initial source size. The effect of the injection shows up at times earlier than ζ ; after $t = \zeta$, the injection rate falls to zero, and $K \propto r^{-2-\gamma}$, the dependence occurring in the conventional formulation of the model. If the transition time ϵ is small compared with the difference $t - \zeta$, then the indicated approximation may be used.

To make the time dependence in equation (2) explicit, I let $r = r_0 + Vt$ where V is the constant expansion velocity. Then, because the adiabatic nature of the expansion implies that $H \propto r^{-2}$,

$$S_\nu = a(t + \rho)^3 \nu^{2.5} [1 - e^{-\tau}] \quad (5a)$$

$$\tau = b(t + \rho)^{-2\gamma-3} \nu^{-(\gamma+4)/2} f(t) \quad (5b)$$

where $\rho = r_0/V$, and

$$a = a_\gamma (10^{-30}) (r_0/R)^2 H_0^{-1/2} \rho^{-3} (10^9)^{2.5} 10^{23} \quad (6)$$

$$b = b_\gamma (0.038) (3.5 \times 10^9)^\gamma r_0 k H_0^{(\gamma+2)/2} \rho^{2\gamma+3} (10^9)^{-(\gamma+4)/2} \quad (7)$$

Equation (5) is in convenient form for least squares fitting. The coefficients a and b are adjusted so that in equation (5) the frequency must be in GHz and the flux density in f.u. The time, t , is actually the difference $t' - t_0$, where t' is the time of observation and t_0 is the initial time. t_0 is interpreted as the time when the model becomes applicable. t and ρ must have the same units of time, in this case days.

Fit to the Data

The results of model fitting to the data at 2.7 and 8.085 GHz (ref. 5) are presented here. Having been taken simultaneously, the flux density readings at these two frequencies do not raise the difficulty of coordinating data at several frequencies at differing times in the equations. Least squares fitting of equation (5) for the parameters ζ , ρ , a , and b for a matrix of values for γ and t_0 leads to the following results:

$$\gamma = 1.7$$

$$t_0 = 0.4 \text{ (September 2, 0930 UT)}$$

$$\zeta = 1.16 \text{ (September 3, 1430 UT)}$$

$$\rho = 1.85$$

$$a = 0.068$$

$$b = 2.1 \times 10^4$$

The root mean square deviation calculated for this fit was 0.65 f.u. γ and t_0 were varied in steps of 0.05 in arriving at these values. $\gamma = 1.7$ corresponds to a spectral index of $\alpha = -0.35$ for a transparent synchrotron source with a power-law spectrum $S \propto \nu^\alpha$. The initial time, t_0 , is 0.4 day past 0 h UT, September 2, which was taken as a convenient reference time. The injection time, ζ , shows that particles were being injected into the source for more than a day after t_0 . For the initial development of the source, injection is an important process.

The parameter ϵ does not appear in the above list of least squares determined parameters because it drops from the equations in the quick transition approximation of equation (4). The validity of this approximation is supported in the improved root mean square generated by successively smaller ϵ values employed in making fits using the exact expression; smaller values for ϵ improved the least squares fit by giving slightly smaller root mean square values down to the limits set on the exponential routine by the computer. If the selected form for the injection rate is correct, then the discontinuous transition from a constant injection to zero, and not a slow fall off in the injection rate, must be considered in interpreting the origin of the injection.

In Fig. 1 I display the data points at 8.085 and 2.7 GHz as well as the least squares determined flux density curves. The model's easy reproduction of the observed peak value in the flux density at the high frequency confirms the importance of a prolonged injection. A plot of the opacity, equation (5b), with the least squares determined parameters (Fig. 2), shows the behaviour of the self-absorption process in the source. At the low frequency, the opacity remains just greater than one until the flux density peaks; the source is initially weakly self-absorbed at this frequency. At the higher frequency, the opacity never exceeds unity; the density of electrons never got high enough to cause self-absorption at this frequency. The effect of internal structure, which is most likely due to inhomogeneities in the magnetic field, shows up at the high

frequency because the source was always transparent there: at least two peaks may be made out in the 8.085 GHz flux density data before the injection ends. This additional variation does not appear in the flux density data at the low frequency.

A still more impressive result confirming the importance of injection is the comparison of observed time and value of the flux density maxima at the various frequencies of observation, with the model predictions on the basis of the least squares fit to the data at 2.7 and 8.085 GHz just presented. Table 1 lists these observed and predicted maximum flux density values for 7 frequencies. The more rapid variations in flux at the high frequencies are especially clear at 10.5 and 8.085 GHz; for these two frequencies, maximum flux density values for each of two discernible peaks are given with the corresponding times of maxima. At 15.5 and 6.6 GHz, the other two frequencies for which the source was always transparent, this fine structure does not appear in the data because observations began late at these frequencies. The model does not reproduce the fine structure; it averages over these variations to arrive at a single peak flux density for each frequency. But the agreement of the model with the general behaviour of the data, especially at the high frequencies where the conventional model falls apart, is clear.

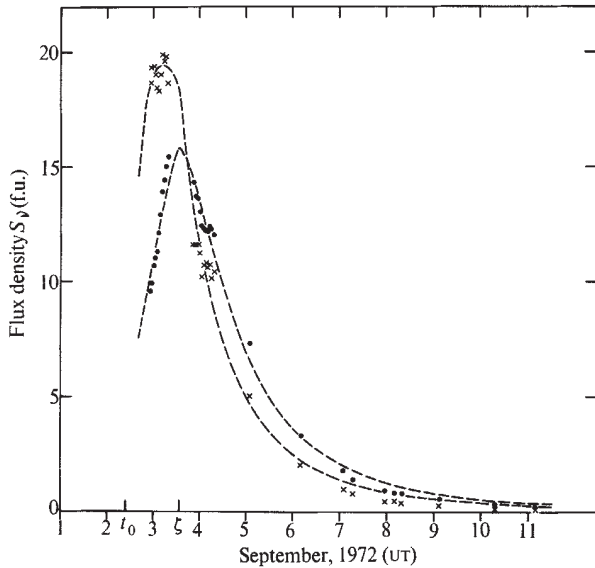


Fig. 1 Cygnus X-3 flux density data and least squares fitted curves at 8.085 (x) and 2.7 (●) GHz. The data were taken from ref. 5.

Physical Conditions of the Cloud; Mass Injection Rate

The parameters ρ , a and b determined in the least squares fit give information about the physical makeup of the expanding cloud. For example, from equation (6), the initial field H_0 may be calculated:

$$H_0 = (10^{-30} a_\gamma / a)^2 (r_0 / R)^4 \rho^{-6} (10^{91}) \\ = 8.2 \times 10^{31} (r_0 / R)^4 \quad (8)$$

where $a_\gamma = 1.22$ for $\gamma = 1.7$. Specification of the initial cloud radius, r_0 , and the distance to the cloud, R , gives H_0 . Although one estimate⁶ put the source between 8 and 11 kpc, no hard data on the source size were collected. Model consistency arguments must be used to set limits on r_0 so that source conditions may be determined.

A lower limit on r_0 follows from the requirement that the

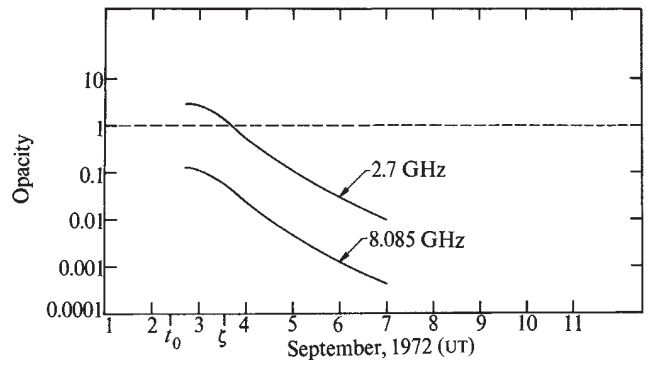


Fig. 2 Synchrotron self-absorption opacity corresponding to the flux density curves in Fig. 1.

Table 1 Observed and Theoretical Values for Flux Density Maxima and Times of Maxima for Seven Frequencies of Observation

Frequency (GHz)	Observed $S_{\max}$ (f.u.)	Observed $t_{\max}$ * (day)	Theoretical $S_{\max}$ (f.u.)	Theoretical $t_{\max}$ * (day)
15.5	16.6	1.22	16.0	1.18
10.5	22.7 (17) 20.9	0.98, 1.23	18.1	1.19
8.085	20.4 (19) 20.2	1.21, 1.32	19.4	1.21
6.6	≥ 22.0	≤ 1.31	20.2	1.25
2.7	16.0	1.5	15.8	1.56
1.68	7.2	2.3	9.1	2.2
0.41	2.0	5.25	1.8	5.4

* Measured from 0 h UT, September 2.

The theoretical values are those predicted from a least squares fit to the data at 8.085 and 2.7 GHz. Observed $S_{\max}$ and $t_{\max}$ values are taken from ref. 8 (15.5 GHz), ref. 9 (10.5, 6.6 GHz), ref. 5 (8.085, 2.7 GHz), ref. 10 (1.68 GHz), and ref. 11 (0.41 GHz). Corresponding to the double peaks in flux discerned at 10.5 and 8.085 GHz, two values each for observed $S_{\max}$ and $t_{\max}$ are listed; the numbers in parentheses indicate the minimum between peaks. The low flux maximum reported at 1.68 GHz is most probably the result of subtracting out too high a base level.

plasma associated with the injected relativistic electrons be rarefied enough to be transparent to the synchrotron radiation generated in the cloud. If the plasma has electron density n_{p1} and magnetic field H , then frequencies ν_0 , of synchrotron radiation for which

$$\nu_0 > 20 n_{p1} / H \quad (9)$$

are observable⁴. This limitation merely backs up the assumption that self-absorption by the relativistic electrons is the only mechanism which renders the cloud opaque to its own radiation. Other limitations on the plasma density (for example, thermal opacity, bremsstrahlung losses) are, it turns out, not as stringent.

The density of relativistic electrons injected into the cloud is determined by integrating equation (3) over energy between the cutoff energies E_1 and E_2 , the energies of the highest and lowest energy electrons in the cloud:

$$n(t) = \int_{E_1}^{E_2} n(E, t) dE = K (E_2^{1-\gamma} - E_1^{1-\gamma}) / (1 - \gamma) \quad (10)$$

Because for each electron energy $E = E_0(r_0/r)$, and because an electron of initial energy, E_0 , radiates most strongly at frequency $\nu = 6.27 \times 10^{18} H_0 E_0^2$ Hz,

Table 2 Values for Several Source Properties for Five Assumed Initial Source Radii

r_0	1.5×10^{14}	2×10^{14}	2.5×10^{14}	3×10^{14}	3.5×10^{14}
Magnetic field strength	0.017	0.054	0.13	0.28	0.51
Relativistic electron density	1.7×10^5	2.3×10^4	4.8×10^3	1.4×10^3	460
Energy in magnetic field	7.2×10^{38}	1.7×10^{40}	2×10^{41}	1.5×10^{42}	8×10^{42}
Energy in relativistic electrons	3.3×10^{44}	5.9×10^{43}	1.6×10^{43}	5.2×10^{42}	2.1×10^{42}
Expansion velocity	0.031c	0.042c	0.052c	0.063c	0.073c

With the exception of those for the initial radius, r_0 , and the constant expansion velocity which applies throughout source evolution, the values correspond to possible descriptions of the source at 1.2 day into source evolution, when particle injection ends. All quantities are in c.g.s. units except where otherwise indicated.

$$n(t) = K(v_1/(6.27 \times 10^{18} H_0))^{(1-\gamma)/2} (r/r_0)^{\gamma-1}$$

$$\text{where } F_v = ((v_2/v_1)^{(1-\gamma)/2} - 1)/(1-\gamma) \quad (11)$$

The density of relativistic electrons maximizes near $t = \zeta$, when all the electrons have been injected into the source:

$$n(\zeta) = k(\zeta)(v_1/6.27 \times 10^{18} H_0)^{(1-\gamma)/2} (1 + \zeta/\rho)^{\gamma-1} F_v \quad (12)$$

The maximum allowable plasma electron density consistent with equation (9) occurs when $n_{pl} = n(\zeta)$. Thus, from equations (9) and (12), the condition which gives the minimum source radius is

$$v_0 H/20 > k(\zeta)(v_1/(6.27 \times 10^{18} H_0))^{(1-\gamma)/2} (1 + \zeta/\rho)^{\gamma-1} F_v \quad (13)$$

The expression defining the lower limit on r_0 results on substituting from equations (4), (6) and (7):

$$r_0^{11} > \left(\frac{a}{1.22 \times 10^{-30}} \right)^5 \left(\frac{b}{3.22 \times 10^{14}} \right) \rho^{-2\gamma+12} (10^9)^{(\gamma-21)/2} (10^{23})^{-5} \\ \times \left(\frac{20}{v_0} \right) \left(\frac{v_1}{6.27 \times 10^{18}} \right)^{\frac{1-\gamma}{2}} \left(\frac{\zeta}{\rho + \zeta} \right) R^{10} F_v \quad (14)$$

where $b_\gamma = 0.506$ for $\gamma = 1.7$ has been used. Values for v_1 , v_2 , v_0 and R must be chosen, the least squares fitted parameters having already been determined. The large power on r_0 makes it practically insensitive to choice of v_1 , v_2 and v_0 . I let $v_1 = 10^7$ Hz and $v_2 = 10^{11}$ Hz, corresponding to wavelengths in the radio range. The lowest frequency at which the source was observed was 0.4 GHz; I set $v_0 = 10^8$ Hz. For $R = 10$ kpc, the lower limit on the source radius must be: $r_0 > 1.6 \times 10^{14}$ cm.

An upper limit on r_0 follows from the condition that there be more energy in the relativistic electrons than in the magnetic field so that the field does not confine the electrons:

$$u_e > H^2/8\pi \quad (15)$$

where u_e represents the energy density in the relativistic electrons. A second lengthy derivation beginning with the determination of u_e from equation (3), leads to the result

$$r_0^{17} < \left(\frac{a}{1.22 \times 10^{-30}} \right)^8 \left(\frac{b}{3.22 \times 10^{14}} \right) \rho^{-2\gamma+21} (10^9)^{(\gamma-36)/2} \\ \times (10^{23})^{-8} \zeta \left(\frac{v_2}{6.27 \times 10^{18}} \right)^{\frac{2-\gamma}{2}} R^{16} \left[\frac{1 - \left(\frac{v_1}{v_2} \right)^{\frac{2-\gamma}{2}}}{2-\gamma} \right] \quad (16)$$

Again, for $R = 10$ kpc, and v_1 and v_2 equal 10^7 and 10^{11} Hz respectively, the upper limit is $r_0 < 3.2 \times 10^{14}$. This maximum radius is smaller by more than an order of magnitude than the maximum set by the time scale for the flux variation.

With these limits on r_0 , it is possible to fill out the description of the cloud. Equation (8) leads to the following limiting values for the initial magnetic field (in gauss):

$$0.062 < H_0 < 0.97$$

The number of electrons injected into the cloud is calculated from equation (12) with appropriate substitutions:

$$N = \frac{4}{3} \pi \left(\frac{a}{1.22 \times 10^{-30}} \right)^3 \left(\frac{b}{3.22 \times 10^{14}} \right) \rho^{-2\gamma+6} (10^9)^{(\gamma-11)/2} \\ \times (10^{23})^{-3} \zeta F_v r_0^{-4} R^6 \left(\frac{v_1}{6.27 \times 10^{18}} \right)^{\frac{1-\gamma}{2}} \quad (17)$$

For the usual values of R , v_1 and v_2 , the maximum number of injected electrons (corresponding to $r_0 = 1.6 \times 10^{14}$ cm) is: $N = 8.9 \times 10^{48}$. For this situation, for which r_0 is minimum, the maximum electron number is also the maximum number of protons in the accompanying plasma, so we also have an upper limit on the mass of the injected cloud: $M < 0.76 \times 10^{-8} M_\odot$. Thus, the maximum possible rate at which mass was injected into the cloud, according to this model, is

$$\frac{dN}{dt} < 0.65 \times 10^{-8} M_\odot \text{ day}^{-1}; \quad t < 1.16 \text{ day}$$

These calculations are summarized in Table 2 with derived values for other source properties. The expansion velocity listed in the table is determined from the parameter $\rho = r_0/V$. Because it is only a small fraction of the light speed, c , the tabulated source properties require no correction for relativistic expansion.

Another Possible Absorption Mechanism

A development which the model is unable to reproduce is the observed evolution of the spectral index α . Both the observations and the model curves show that the source became transparent at the lower self-absorbed frequency when the flux maximized at that frequency. For a transparent synchrotron source, the spectral index, α , is expected to be constant. But from at least September 4 to 6, while the source was transparent at both frequencies, the observations at 2.7 and 8.085 GHz show that the spectral index measurably evolved to its final constant value⁵. Because the source was already transparent at both frequencies well before this evolution occurred, the phenomenon cannot be explained by optical

depth effects. There is also evidence for evolution in α at still higher frequencies. Data at 8.0 and 15.5 GHz (ref. 7) show that the spectrum steepened from $\alpha = -0.44$ to $\alpha = -0.71$ between September 3 and 4. At these frequencies, the source was always transparent so that the question of possible optical depth effects does not even arise. Some additional process must have been at work.

One such process might be absorption of radiation by a plasma. Synchrotron radiation in a rarefied plasma would show a flux density depressed at low frequencies relative to what would be observed for radiation *in vacuo*. Looking at the 8.085 and 2.7 GHz data, I surmise that if the observed 2.7 GHz radiation is to some extent depressed, then α should be closer to zero, less negative than if the particles were radiating *in vacuo* and none of the radiation was suppressed. A larger flux density at the low frequency, than that observed, would change the spectral index in the direction of a larger negative index; that is, toward the constant value one would expect for a transparent source of electrons radiating in a vacuum. The fact that the spectral index evolved up to about September 6 at 8.085 and 2.7 GHz, and was constant after September 6, can be explained by arguing that the plasma was dense enough before September 6 to have noticeable effect and, after September 6, rarefied enough so that its effect dropped from view. If the spectral evolution does find its explanation in this argument, then the turnover in flux density at low frequencies is caused not by synchrotron self-absorption, but by absorption

of the radiation in a dispersive medium⁴, the so-called Razin-Tsytoovich effect.

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Non-equilibrium Isotopic Fractionation between Seawater and Planktonic Foraminiferal Tests

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Planktonic foraminiferal tests are not formed in isotopic equilibrium with seawater; the deviation is species dependent.

UREY¹ has suggested that the temperature dependence of the isotopic fractionation factor between the oxygen in water and the oxygen in calcium carbonate could be used as a geological thermometer. For estimating Earth surface temperatures, biologically deposited calcium carbonate is more widely available than inorganic precipitates. So it was necessary to discover whether or not organisms deposit carbonate under equilibrium conditions. Epstein *et al.*^{2,3} investigated this using molluscs; although they found one case where a mollusc seemed to have deposited some carbonate in non-equilibrium conditions, they ascribed this to special circumstances. Apart from this one case, they inferred that the Mollusca deposit calcium carbonate in isotopic equilibrium with the surrounding water.

Until recently it has been assumed that this is also true of the Foraminifera. Support for this assumption comes from the

seemingly reasonable temperature values which Emiliani^{4,5} derived making this assumption. Indeed, whereas the first work on molluscs was performed with the intention of investigating the isotopic fractionation as a function of temperature, the first work on planktonic foraminifera⁶ was an investigation of the depth (temperature) habitat of recent foraminifera, performed on the assumption that the isotopic fractionation factor was known. We now find that this was an unwarranted assumption, and that a substantial portion of the variation in isotopic composition between one species and another in foraminiferal death assemblages is due to different fractionation factors rather than to different life habitats.

Oxygen Isotope Analyses

Duplessy *et al.*⁷ have previously reported differential isotopic fractionation among benthonic foraminiferal species, and van Donk⁸ obtained evidence suggesting that the planktonic species may also deposit calcite out of equilibrium with water. But although a fossil population such as that studied by Duplessy *et al.* enables a comparison to be made between benthonic species, it cannot be used for planktonic species because they do not derive from the same temperature habitat. For this rea-

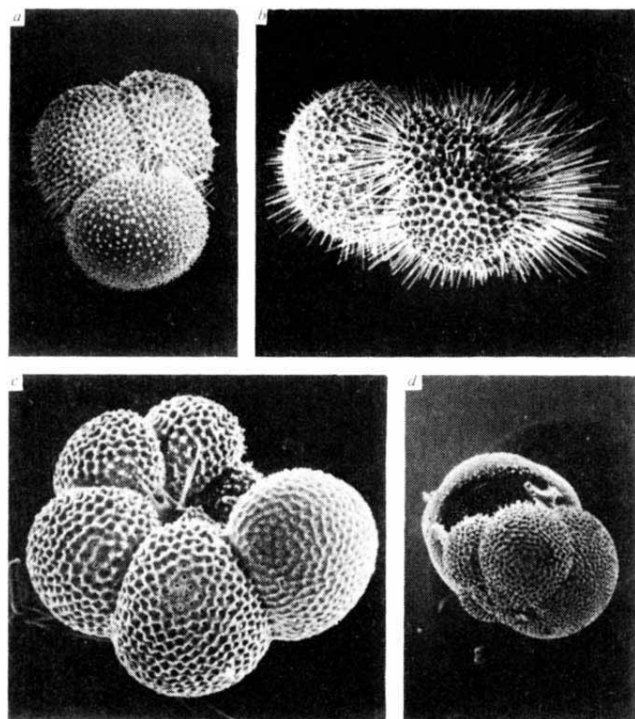


Fig. 1 Electron scanning micrographs of planktonic foraminifera from a 50 m horizontal tow (16° 38' S, 113° 03' E). a, *G. ruber* ($\times 65$); b, *G. sacculifera* ($\times 65$); c, *G. dutertri* ($\times 120$); d, *P. obliquiloculata* ($\times 65$).

son, it is only possible to compare the departure from isotopic equilibrium among planktonic species if they are collected in plankton tows within the isothermal layer of the ocean.

With the exception of a few samples analysed by van Donk all oxygen isotope analyses of planktonic foraminifera so far published have been performed using fossil or sub-fossil material. The reason is that it is in general difficult to collect large enough samples from plankton tows for conventional isotope analysis. In the present work we have been able to analyse samples as small as 0.04 mg carbonate, and so have been able to make use of a series of plankton tows made in the Indian Ocean by US Coastal and Geodetic Survey Ship Oceanographer in 1967. The stations from which we have used samples in this study are given below in Table 1. Some samples are shown in Fig. 1.

Table 1 Sites of Sampling Stations 150 m Horizontal Tows

BM number	Station number	Latitude	Longitude
1968,0,433	3	08° 11' N	75° 13' E
1968,0,434	4	06° 52' N	77° 43' E
1968,0,435	5	05° 55' N	80° 07' E
1968,0,436	6	05° 34' N	83° 38' E
1968,0,437	7	05° 26' N	85° 37' E
1968,0,445	15	16° 38' S	113° 03' E

Where possible, the samples for isotope analysis were divided and two independent analyses made. This provides a check on the reproducibility of the analyses, which we considered desirable because plankton have not previously been analysed at the Cambridge laboratory. Samples were roasted *in vacuo* for 30 min at 450° C prior to analysis. Carbon dioxide for mass spectrometric analysis was released by the action of 100% orthophosphoric acid at 50° C. The oxygen isotopic composition of the gas was compared with that of an aliquot from a standard bulk gas sample, using the mass spectrometer described by Shackleton⁹, and the results calibrated by analysing standard carbonates under the same conditions.

In this work Emiliani's belemnite standard B1 has been used as a calibration standard, assuming its ^{18}O content to be $+0.1\text{‰}$ with respect to the PDB standard. Analyses listed in Table 2 are referred to the PDB standard on this basis. PDB is a standard based on a belemnite from the Carolina Pee Dee Formation¹⁰.

Table 2 Oxygen Isotopic Composition (δ , ‰) of Foraminifera (Fig. 1) from Plankton Tows

Station	<i>G. ruber</i>	<i>G. sacc.</i>	<i>G. dutert.</i>	<i>Pull. obl.</i>
3	-2.69	-2.42	-2.27	-2.08
4	-2.77	-2.50	-2.16	-1.98
5	-2.59	-2.55	-2.15	-2.01
6	-2.64	-2.65	-2.37	-2.36
7	-2.65	-2.69	-2.30	-2.22
15	-2.40	-2.28	-2.14	-1.71

Fourteen of these figures are the mean of two independent analyses. The standard error of a single analysis may be estimated from the difference between these pairs as $\pm 0.11\text{‰}$.

Not all the species in each plankton tow sample have the same isotopic composition. We have performed an analysis of variance to isolate between species, between station and residual variation.

Between species variation proves to be highly significant ($P < 0.001$). The Students *T* test was used to test variation between species (Table 3).

Table 3 Variation Between Species

<i>G. ruber</i> $\times$ <i>G. dutert.</i>	$T = 6.903$ DF 15 significant $P < 0.001$
<i>G. ruber</i> $\times$ <i>P. obliqui.</i>	$T = 9.958$ DF 15 significant $P < 0.001$
<i>G. sacc.</i> $\times$ <i>G. dutert.</i>	$T = 4.993$ DF 15 significant $P < 0.001$
<i>G. sacc.</i> $\times$ <i>P. obliqui.</i>	$T = 8.048$ DF 15 significant $P < 0.001$
<i>P. obliqui.</i> $\times$ <i>G. dutert.</i>	$T = 3.055$ DF 15 significant $P < 0.01$

The residual variation is 0.1‰ , which may be compared with the standard deviation of $\pm 0.11\text{‰}$ derived from the pairs of analyses. The apparent difference between *G. ruber* and *G. sacculifera* is only 0.11‰ , too small to be estimated reliably in the present experiment.

Implication for Depth-Habitat Studies

Emiliani⁶, Lidz *et al.*¹¹ and Hecht and Savin¹² have used $^{18}\text{O}/^{16}\text{O}$ ratio determinations in foraminiferal tests as a method of investigating their life habitats. In the course of a study of a core in the Indian Ocean, Oba¹³ did the same for one sample. It is clear from our study that this is not a valid approach; indeed, as regards the four species discussed here the between species differences found in plankton samples from 50 m horizontal tows are indistinguishable from the variations found by Oba in a sediment sample. This means that in all probability none of the variation measured by Oba can be ascribed to different depth habitat among the four species; they all derive from populations living in the isothermal layer.

In the Atlantic province, larger differences between the species have been measured^{6,11,12}; it seems likely that in that case there is a contribution which may be safely ascribed to difference in depth habitat. At the same time we need to know much more about the differential fractionation effect before we can begin to use isotopic determinations in order to deduce life habitat.

Hecht and Savin¹² have gone further, and attempt to use isotopic determinations to discover whether morphological variation within a population of foraminifera is due to varying ecological stress; they deduce, for example, that specimens of *Globigerinoides ruber* with a diminutive final chamber are those

Table 4 Estimated Deviation from Isotopic Equilibrium

Station	Test	Difference between δ_{meas} and δ_{est}					
		$\delta_{\text{west.}}$	$\delta_{\text{cest.}}$	<i>G. ruber</i>	<i>G. sac.</i>	<i>G. dutert.</i>	<i>P. obliqui.</i>
3	27°	+0.1‰	-2.14‰	-0.55	-0.28	-0.13	+0.06
4	27°	+0.1‰	-2.14‰	-0.63	-0.36	-0.02	+0.16
5	27°	+0.1‰	-2.14‰	-0.45	-0.41	-0.01	+0.13
6	27°	0.0‰	-2.24‰	-0.40	-0.41	-0.13	-0.12
7	27°	0.0‰	-2.24‰	-0.41	-0.45	-0.06	+0.02
15	25°	0.0‰	-1.83‰	-0.57	-0.45	-0.31	+0.12
				-0.50‰	-0.39‰	-0.11‰	+0.06‰

which have lived in deeper (colder) water, by comparing their oxygen isotopic composition with that of normal individuals. Although this seems to be an ingenious test, we cannot exclude the possibility that whatever factor influences the shape of the final chamber also influences the departure from isotopic equilibrium in the test carbonate. This is by no means impossible, particularly because the suggestion made by Parker¹⁴, that non-equilibrium isotopic composition could be causally related to the presence of symbiotic zooxanthellae, has never been excluded.

Implications for Palaeotemperature Studies

Because isotope analysis was not envisaged when the samples were collected, we do not have information on the temperature and isotopic composition of the water in which the foraminifera were living. This means that we cannot estimate exactly the isotopic composition which would have been measured had the test carbonate been deposited in isotopic equilibrium; however, an approximate estimate may be made. Craig and Gordon¹⁵ show that in the equatorial region the observed variation in surface isotopic composition with salinity is small, about 0.11‰ for 1‰ change in salinity. Using Defant's¹⁶ plate V, we may assume that at stations 6, 7 and 15 the salinity was in the region of 34.5‰, and that the isotopic composition of the water was near zero on the PDB scale (+0.2‰ on the SMOW scale¹⁵). At stations 3, 4 and 5 the salinity is likely to have been a little higher and the isotopic composition about +0.1‰ on the PDB scale. As regards temperature, the mean August surface temperatures (Defant¹⁶, Plate 3B) are about 27° C for stations 3, 4, 5, 6 and 7, and about 25° C for station 15. Using these estimates and the relation between temperature and isotopic composition given by Craig¹⁷ yields the values in Table 4. Comparison with the measured isotopic composition for each species from Table 2 gives the extent of departure from isotopic equilibrium for each species. The estimates range from -0.50‰ for *G. ruber* to +0.06‰ for *P. obliquiloculata*.

In column 4 of Table 4 the isotopic composition of carbonates deposited at the temperature given in column 2, and in water having the isotopic composition of column 3, is estimated on the basis of the equilibrium relationship of Craig¹⁷. The remaining columns are the differences between the measurements from Table 2 and the values in column 4, and thus represent deviations from isotopic equilibrium for the species concerned.

For this last species, the deviation is insignificant; it may well be that this species does in fact deposit its test in isotopic equilibrium with the surrounding water. If one could extract confidently from the sediment only those tests of *P. obliquiloculata* which lived in the isothermal layer of the ocean, this might well be an ideal species to use for palaeotemperature determination; it is possible that these could be recognized by the lack of the smooth external cortex which is a characteristic feature in tests from deeper water.

At the other end of the scale, *G. ruber* yields a value 0.5‰ lighter than it would if isotopic equilibrium prevailed. This is equivalent to an error of about 2.5° C.

Before these values are used to correct estimates of palaeotemperature, it is important to establish whether the "vital effect"¹ remains constant for each species. We have only measured the effect for foraminifera living at 50 m and in a restricted area of an ocean; it is of great interest to discover whether our results have general application.

It is in any case not possible to use the data to correct measurements made in other laboratories because at present results from different laboratories do not seem to be related to each other. For example, specimens of *Globigerinoides sacculifera* from the top of core P6304-8 gave -1.29‰ when analysed by Emiliani⁶; samples from the same level in the same core gave -1.69‰ when analysed by Lidz *et al.*¹¹ and the same species from nearby core V12-122 yielded -2.2‰ (ref. 18). When corrected for the isotopic composition of the Caribbean water (+0.92‰) these figures yield temperatures from near 27° to near 32° C. At present these differences seem more serious than the fundamental problem posed by the present work.

We conclude that whether the isotopic composition of a foraminiferal test is analysed with a view to determining its present-day life habitat, or with a view to elucidating the mysteries of climatic change in the past, it is not possible to translate the value obtained into an equivalent temperature on the basis of thermodynamic principles alone. In some manner yet to be determined the organism deposits carbonate of isotopic composition differing slightly from the thermodynamically predicted value.

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LETTERS TO NATURE

PHYSICAL SCIENCES

Flying Clocks and the Sagnac Effect

In their "flying clock" experiment¹ Hafele and Keating observed an on-Earth directional dependence of the relativistic time dilation. I have argued² that such a dependence is contrary to special relativity theory; the effect, however, is essentially one involving accelerated motion³ and my neglect of this fact invalidated my argument. None the less, locally the time effects on moving clocks may be regarded as special-relativistic (neglecting the altitude effect, which is not relevant for the present discussion); and the derivation of the effects was made by Hafele with the customary $(1 - v^2/c^2)^{1/2}$ time-rate change factor^{4,5}. A seeming inconsistency then still arises in considering the clocks from the Earth reference frame: if two similar clocks are moving on equatorial paths with equal speeds relative to the Earth, one westward and one eastward, they should have equal time rates and equal kinetic energies in the Earth system. Evidently, they do have equal energies, but not equal time rates. But if the Sagnac effect is taken into account in the synchronization of clocks in the Earth frame the contradiction disappears; one finds, rather, a further exemplar of consistency in the theory of relativity.

With omission of the altitude term, the equation⁴ which was confirmed by the Hafele-Keating observation is

$$\Delta t' \simeq (1 - v^2/2c^2 - vR\Omega/c^2)\Delta t \quad (1)$$

Δt is time interval for a rest Earth clock and $\Delta t'$ is for a clock moving on the equator with speed v , (+) for eastward, (−) for westward motion; Ω is the Earth's axial rotation velocity, and R its radius (to be taken with a $\cos \lambda$ factor for east-west motion at latitude λ).

The Sagnac effect⁶⁻⁸ requires that the time for light to be reflected around a closed path in a system rotating with angular velocity Ω will be longer (shorter) by $2A\Omega/c^2$ than when $\Omega=0$, if the sense of the path is the same as (opposite to) that of Ω ; A is the area enclosed by the light path. Synchronizing rest clocks along the equator, using the Einstein procedure⁹, requires that $t_2 - t_1 = L/c$, where t_2 and t_1 are reception and emission times, respectively, for a light signal sent the Earth distance L from clock "1" to clock "2". For signals directed eastward, additional time $2\pi R^2\Omega/c^2$ will be required for traversal around the Earth, compared with the time that would be given by clocks in a hypothetical non-rotating Earth system S . Hence the equatorial clocks fall behind, compared with S clocks, as we progress eastward; the Earth observer, using the $\Delta t = L/c$ criterion, does not take into account the increase in light path that results from the Earth's axial rotation. (The equatorial rest clocks also are presumably running slow by a uniform $\Omega^2 R^2/2c^2$ factor, compared with the S clocks.)

In moving a distance $\Delta x = v\Delta t$ the eastward flying clock should lose $(v^2/2c^2 + vR\Omega/c^2)\Delta t$ s compared with Earth rest clocks. But if these are synchronized by the Einstein procedure, an eastward displacement of Δx gives a fraction $\Delta x/2\pi R$ of the $2\Omega A/c^2$ Sagnac loss, which is, using $A = \pi R^2$, a loss of $(\Omega R/c^2)\Delta x$. This decrease is the same as the loss, $(vR\Omega/c^2)\Delta t$, $\Delta t = \Delta x/v$, that is prescribed by equation (1). Hence, the Earth observer will not see a direction time change for the moving clock, but only the kinetic $(v^2/2c^2)\Delta t$ loss. Similarly for a

clock moving to the west: the $(+vR\Omega/c^2)\Delta t$ gain will be compensated by the increase that the Sagnac effect gives to the synchronized clocks. For the Earth observer, then, each flying clock loses time only by the $-v^2/2c^2$ factor.

But at some point there must be a discontinuity of $2A\Omega/c^2$ in the equatorial clock system, because the Sagnac effect puts that loss (gain) into an eastward (westward) synchronization around the equator. The $(vR\Omega/c^2)\Delta t$ term of equation (1), with $\Delta t = 2\pi R/v$ for a circumnavigation of the Earth, also gives the time difference $2\pi\Omega R^2/c^2 = 2A\Omega/c^2$, in exact agreement with the synchronization discontinuity. Also, we see from the last calculation that the difference is independent of the speed v at which the clock is moved. Hafele and Keating did confirm a $\pm 2A\Omega/c^2$ time difference (~ 200 ns, $\lambda=0$) for clocks carried around the Earth, compared with a rest clock.

For equatorial clocks set by meridian transit of star (in effect, synchronized with S coordinate clocks), the east-west time effect will appear. With Einstein synchronized clocks there would be no directional effects along a given line of latitude, but there would be what we might call the Hafele-Keating discontinuity, of magnitude $2A\Omega/c^2$ and, like the International Dateline, required for single valued time measure. Because A varies with $\cos^2 \lambda$, a continuous change of time would then also be required along each line of longitude. There would be no physical basis in north-south signal propagation for this last time variation. But with any idealized spherical Earth time-mesh there would be a north-south signal insensitive discrepancy; a $(1 - \Omega^2 R^2 \cos^2 \lambda/c^2)^{1/2}$ clock-rate slowing factor that is uniform at any given λ . Seemingly, the asymmetry in clock synchronization that comes with the Earth's axial rotation cannot be escaped.

I thank Professor Peter D. Noerdlinger for a conversation in which he suggested the role of the Sagnac effect elaborated in this letter.

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Possible Marginal Fracture Ridge south of South Africa

A NOTABLE feature of the continental margin south-east of South Africa is its steep slope. Off the west coast of South Africa, north of Cape Town, a thick wedge of sediments has given the slope a gentle gradient of about 1.5° (ref. 1), while southwards from Cape Town the gradient is about 5°. But when the slope turns abruptly (at the tip of Agulhas Bank,

Fig. 1) to face the Indian Ocean, a steep "scarp" of up to 10° is encountered. Seismic profiling data, recently collected by the Geological Survey of South Africa, show that between the Agulhas Bank and Port Elizabeth the steep scarp can be directly related to the presence of a basement ridge beneath the continental slope.

Nine seismic reflexion profiles across the continental margin (Fig. 1) clearly show the nature of the basement ridge. Three of the profiles, numbers 2, 5 and 9, are presented in Fig. 2 as interpretative line diagrams. The ridge is best developed as such in the vicinity of profiles 3, 4 and 5, where it divides the slope into an upper sediment terrace and a lower basement scarp. It reaches a width of about 40 km in this area, and its crest consists of a number of peaks, usually three. It has no magnetic signature. The upper sediment terrace has evolved as a result of the damming effect of the ridge, although on profile 4 sediment seen to be banked up against the southward facing scarp may have spilled over the barrier. Seawards, the basement scarp drops down to a poorly developed continental rise, where a chain of seamounts and small basement peaks runs parallel with the continental slope. Our profiles do not show the relationship of the basement ridge to this seamount chain, but an interpretation of magnetic data (A. P. and E. S. W. Simpson, unpublished) indicates that the boundary between continental and oceanic crust (named the Agulhas Fracture Zone by K. O. Emery, private communication) may run between the two features. The ridge therefore seems to be a basement high associated with the continental crust.

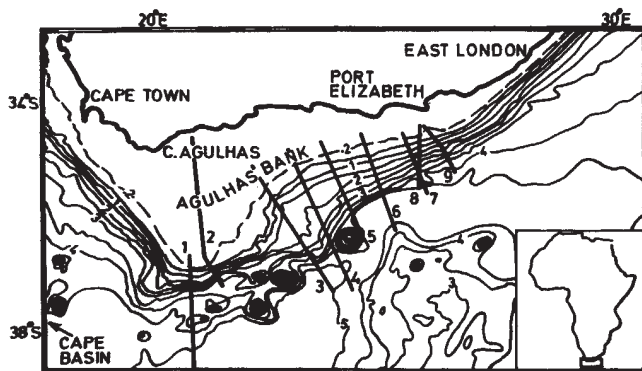


Fig. 1 Bathymetric map of the continental margin south of South Africa. Isobaths are drawn at 200 m and thereafter at 500 m intervals; depths given in km. Locations of the continuous seismic profiles 1 to 9 are marked. Inset shows the position of the area with respect to Africa.

Profiles 6 to 9 show that the crest of the ridge becomes deeper towards the north-east. South of Port Elizabeth it lies at about 3 km below sea level. Between Port Elizabeth and East London, a change in the topography of the lower slope, from being convex in profile to being concave, suggests that the ridge may disappear completely in this region or continue as a very small feature. A linear positive magnetic anomaly, caused by the juxtaposition of continental and oceanic crusts, converges on the ridge east of Port Elizabeth. South-westward from profile 3 the trend of the top of the basement scarp is inferred from bathymetric data until profile 2 is reached. Here the basement rises very steeply to within 1 km of the sea surface before disappearing beneath the sediment cover on Agulhas Bank. At the bottom of the continental slope, basement is lost beneath a trough of sediments presumably associated with the Agulhas Fracture Zone.

We consider the relationship of the newly discovered ridge to the Agulhas Arch², a basement antiform trending south-eastwards from Cape Agulhas. Fig. 3 shows the outcrop area of the Palaeozoic and Precambrian rocks forming the Arch and isopachs of the approximate depth to basement below sea

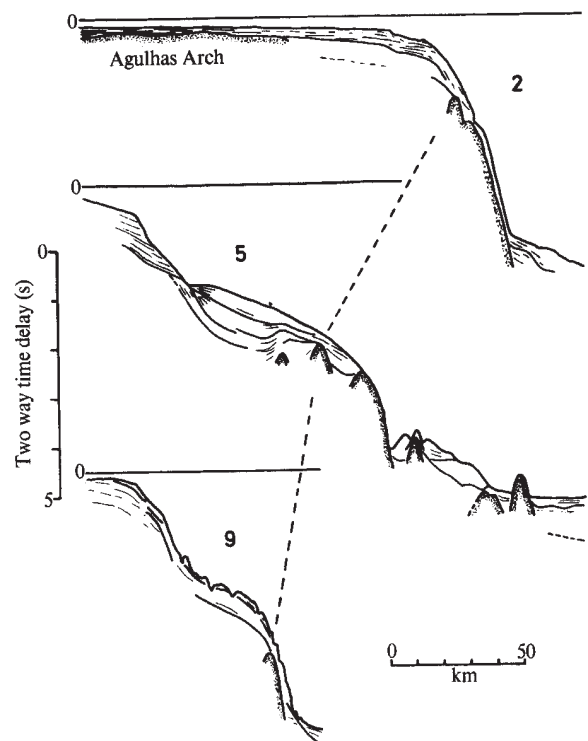


Fig. 2 Interpretative line diagrams of the southern part of profile 2, profile 5 and profile 9. Basement features are stippled. A dashed line correlates the possible marginal fracture ridge from profile to profile.

level in the sediment covered areas (data taken from refs. 2-5 and profile 2). The Arch seems to continue south-eastwards at a fairly shallow depth, less than 1 km, until it meets the basement ridge. Where the two meet, the continental slope is extremely steep, probably as a result of the effect of the Arch on the formation of the ridge. Therefore the two positive features together form a continuous basement high, surrounding the Agulhas Bank and increasing in depth from near sea level at Cape Agulhas to 3 km below sea level near Port Elizabeth. This is an excellent example of a sediment dam^{6,7}, without which the deep sedimentary basin on the Agulhas Bank^{3,8} may not have developed to its present size.

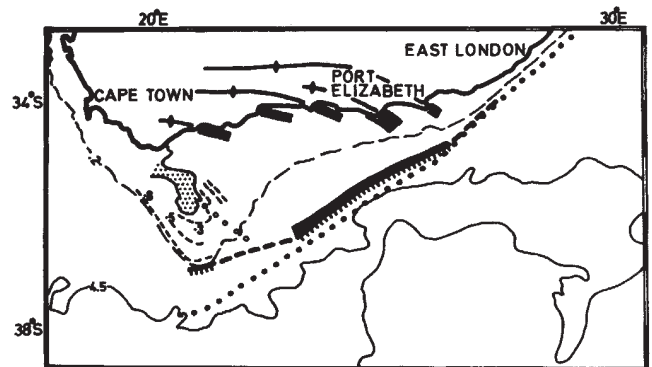


Fig. 3 Structural framework of the continental margin south of South Africa. 200 m and 4.5 km isobaths are shown. Basement ridges have been continued offshore with the aid of seismic data³. Magnetic trends taken from unpublished data of A. P. and E. S. W. Simpson. —, Anticlinal axis; ---, basement ridge; - - - - -, marginal fraction ridge; - - - - -, inferred ridge; stipple, Agulhas Arch outcrop; . . . , strong magnetic trend; ○○○, weak magnetic trend; depth below sea level (km) to Agulhas Arch marked on contours.

Although there seems to be physical continuity between the ridge and the Agulhas Arch, the age and composition of the former are unknown. Its trend, parallel to the continental edge and oblique to basement trends inshore, suggests an origin associated with the formation of the continental margin. According to a structural model proposed for the South Atlantic^{9,10}, the margin formed as a line of shear. This took place during the initial opening of the South Atlantic, say between 130 m.y. and 100 m.y. ago, when the Falkland Plateau slid past the Agulhas Bank producing the Agulhas Fracture Zone. On this basis, a Lower Cretaceous age is indicated for the formation of the ridge. The material comprising the ridge could be a splinter of pre-Cretaceous continental basement, perhaps originally attached to the Falkland Plateau. Seismic work has shown that continental rocks underlie the Plateau and its steep northern scarp¹¹. Alternatively, the material may be typical of a type of marginal fracture ridge⁹, like the Ivory Coast-Ghana Ridge, which is associated with the Romanche Fracture Zone¹². Structurally, our ridge and the Ivory Coast-Ghana Ridge look similar, and both are magnetically quiet. But the two differ in that our ridge appears to peter out beyond Port Elizabeth instead of running the full length of the continental margin offset (Agulhas Bank to Durban¹⁰). As a possible explanation for this we suggest that the nature of the continental rocks against which the ridge is formed is a factor governing the size of the ridge. The petering out may then be due to the fact that just north of Port Elizabeth the Cape Fold Belt, underlain by Precambrian basement, dips beneath flat-lying Karroo (Carboniferous to Jurassic) sediments. It may be that the Ivory Coast-Ghana Ridge is better developed because it formed against Precambrian basement throughout its length. An alternative explanation is that our ridge was originally all at one depth but has since sunk differentially.

As yet it is not known if the trend of the newly discovered ridge is continued beneath the sediments of the Cape Basin. Le Pichon and Hayes's theory⁹ predicts that a basement high should exist there. Before being sure that we have discovered a true marginal fracture ridge, it is necessary to survey the Cape Basin and satisfactorily explain the petering out beyond Port Elizabeth.

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Palaeolimnology and Palaeomagnetism

MAGNETIC studies of freshwater sediments from northwest England and Northern Ireland have revealed a wide range of applications of magnetic measurements to palaeolimnological studies. They have also shown that lacustrine sediments give a unique record of past changes in the geomagnetic field. This letter is chiefly concerned with the uses of magnetic measurements in helping to interpret lacustrine successions; Creer *et al.*¹ have already discussed the implications of the secular changes of the Earth's magnetic field as recorded in the sediments of Lake Windermere.

The magnetic parameters which have contributed in helping to decipher the information locked in lake deposits are declination, inclination and intensity of the natural (NRM) and cleaned magnetic remanence; initial susceptibility; and response of NRM intensity to a variety of thermoremanent and thermomagnetic tests. Variations in declination with depth can be used to date the sediments. Initial susceptibility and intensity measurements are useful for fine correlations between cores from the same lake, and also provide information about processes which have been operating in the lake's drainage basin. Other magnetic studies have provided information principally about the origin of the material holding the NRM. Instruments have recently been developed at Newcastle to measure the important properties of magnetic declination and its intensity^{2,3} and initial susceptibility (L. Molyneux and R. T., unpublished) on whole lengths of core. All samples were collected by Mackereth pneumatically operated piston corers of either 1, 3 or 6 m length^{4,5}.

The record of secular variation for Lake Windermere is accurately known for the past 11,000 yr (Fig. 1) with a time scale provided by a suite of radiocarbon dates. Fourier and spectral analyses of the results revealed a single significant periodicity of about 2,800 yr in the declination variations, but

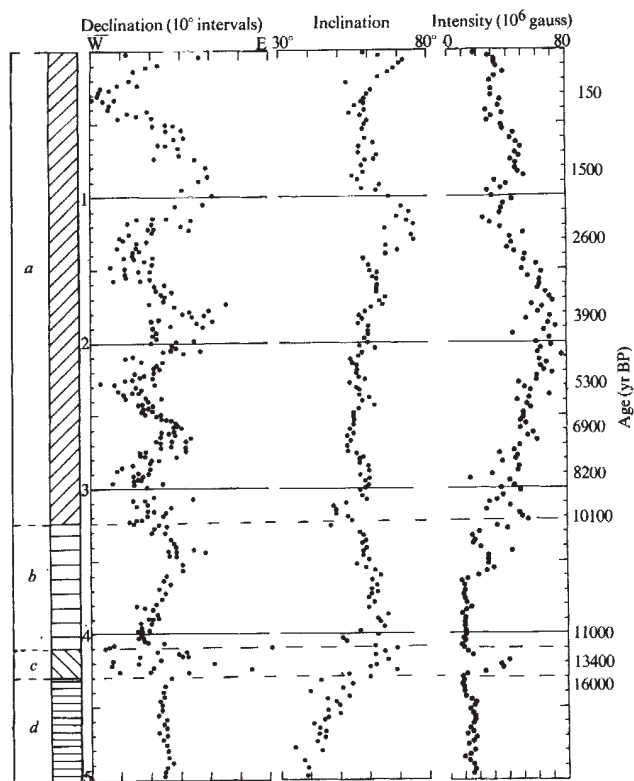


Fig. 1 Composite plot of stratigraphy: declination, inclination and intensity of the NRM versus depth in metres from four 6-m cores of sediment from Lake Windermere. Ages from Mackereth⁶. Relative, rather than absolute, values of declination are plotted. a, Post-glacial organic; b, late glacial laminated clays; c, amelioration period; d, glacial varved clay.

none in the inclination changes (Fig. 2), confirming Mackereth's conclusion⁶ that the oscillations in declination were of constant frequency. Comparison of detailed measurements from the top metre of sediment in Windermere with observatory and archaeomagnetic results for the past 500 yr showed that the NRM became stabilized soon after the time of deposition of the sediment, and alternating field cleaning showed that the NRM was of high stability¹. Thus the Windermere record of declination changes (Fig. 1) provides a reference curve which can be used to date other lacustrine successions simply on their variations in declination of magnetic remanence.

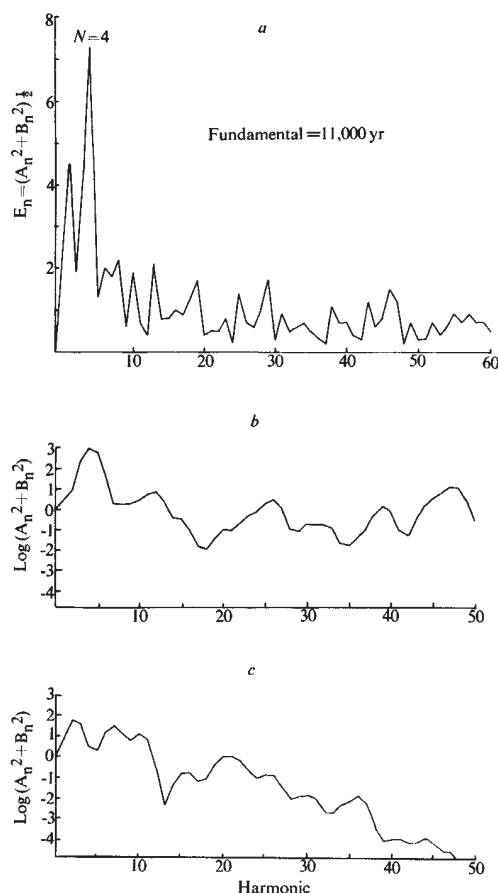


Fig. 2 Lake Windermere. *a*, Fourier analysis of the declination record; *b*, spectral analysis of the declination record; *c*, spectral analysis of the inclination record.

One 6-m and eight 3-m cores from Lough Neagh were provided by F. Oldfield for magnetic measurements from a larger collection intended for palaeobotanical studies. Carbon 14 ages have been assigned to core AB9 by correlating its pollen assemblages with those of another Lough Neagh core which had been isotopically dated. Only the carbon 14 ages of 4,800 and 3,400 BP are now thought to be reliable estimates of the sediment age. These ages compare well with the palaeomagnetic dates (Fig. 3*a*). Further, pollen analyses yield an age of about 6,000 BP for the basal material in core AB9, in good agreement with the magnetic age. Other cores gave similar swings in declination (Fig. 3*b, c*) indicating comparable rates of deposition to those in core AB9, but one core (AB11) held more swings in declination than the other cores (Fig. 3*d*). Comparison with the Windermere reference curve suggests an age of about 9,000 yr BP for the oldest sediment in this core, and shows that the rate of deposition has been markedly slower in the lower half of the core compared with the upper part. Pollen analyses conform remarkably well to this pattern and time scale of deposition⁸.

Mackereth (personal communication) showed that the horizontal intensity of the NRM in Windermere was related

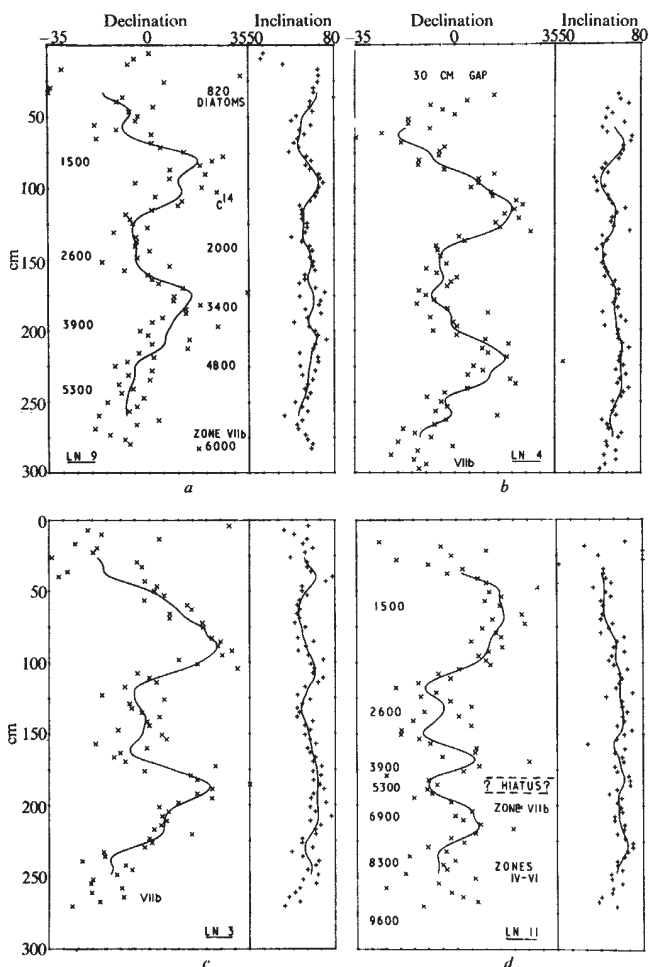


Fig. 3 Declination and inclination changes for four 3-m cores from Lough Neagh. In diagram *a* the left hand dates are derived by comparison with the Lake Windermere magnetic record, the right hand dates are from Lough Neagh. In diagram *d* the dates are derived from the Lake Windermere magnetic record.

to the carbon content of the sediments. Measurement of the total intensity of NRM of both Lough Neagh and Lake Windermere sediments again produced the same relationship of direct proportionality between carbon content and intensity. This is a clear indication that the intensity of the remanence was controlled by biological activity in the lake and in particular in the soils of the surrounding areas, rather than by changes in intensity of the geomagnetic field. There is an inverse correlation between the mineral content of the lake sediments and the intensity of their magnetization. For example, in both Lake Windermere (Fig. 1) and Lough Neagh the intensity of NRM reached a maximum in mid-Post-Glacial times, when erosion was at a minimum, but leaching of soils and lake productivity were at a maximum⁹. Thus the remanence is of a chemical, as opposed to a depositional, origin. Low temperature transition studies have shown that the NRM is largely carried by haematite¹.

Initial (low field) susceptibility measurements were made on all the subsamples from the Lough Neagh cores. Sediments from deeper water areas had lower values and smaller fluctuations of susceptibility than the cores from the shallower water nearer the edge of the Lough. The changes in susceptibility of the deep water cores (Fig. 4) were similar from core to core and give a method of accurate correlation between cores in the Post-Glacial organic material, which without detailed analysis seems homogeneous. Correlation with the shallow

water cores is also possible but it is not as precise. Oldfield (personal communication) has demonstrated that the course of susceptibility change (Fig. 4) closely parallels the sequence of forest clearance in the Lough Neagh drainage basin, as reflected in the grass, bracken and rib-wort plantain pollen content of the cores. This aspect of the palaeolimnological work is being pursued in greater detail by magnetic, chemical and botanical investigations of the most recent sediments in Lough Neagh.

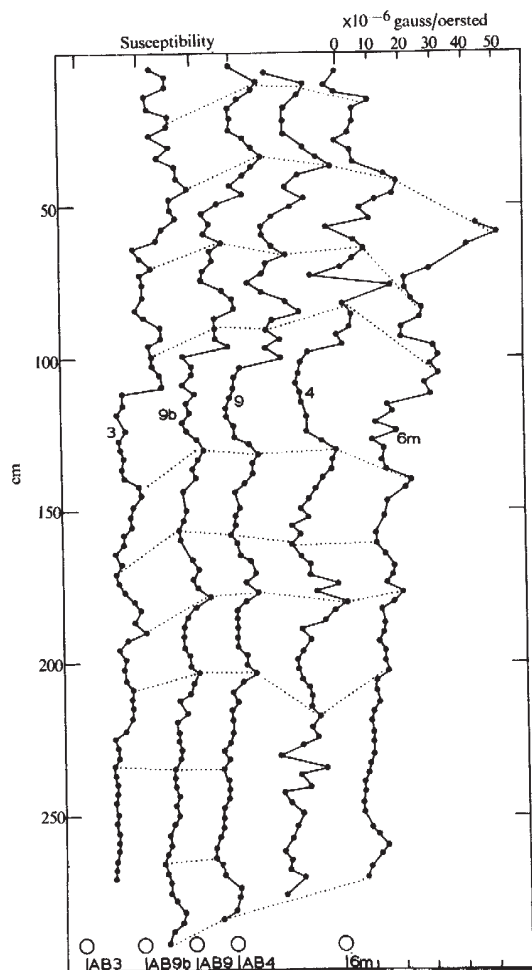


Fig. 4 Susceptibility against depth for the deep water Lough Neagh cores. Susceptibility is plotted on a linear scale; the origin of the susceptibility scale for each core is indicated along the bottom axis. Correlations between cores are shown by the dotted lines. (For comparison with Fig. 3 add 40 cm to depths in core AB4.)

The detailed information about the past changes of the geomagnetic field obtained from Lake Windermere sediments can thus be used to help in the investigation of other Post-Glacial lacustrine deposits. Measurements of changes in declination, particularly using the whole core method, form an extremely rapid dating technique. Declination and intensity variations are useful as reconnaissance tools for providing, nondestructively, stratigraphical information about cores before more detailed and time consuming investigations are carried out. Susceptibility and declination changes give a means of correlating accurately between cores from the same lake. Information about the sediment type, and the biochemical conditions in which it was formed and deposited, are provided by the magnitude of initial susceptibility and intensity of NRM. Present studies on lacustrine sediments from a

previous (Hoxnian) interglacial period indicate that the work can be extended further back into the Pleistocene.

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Radiometric Traverse of the Seabed off the Yorkshire Coast

SURFACE and airborne radiometric surveys carried out over land areas during the past twenty years have shown that in addition to locating radioactive mineral deposits they are able to differentiate between the common types of rocks and sediments. As yet, however, few attempts have been made to extend radiometric techniques to the sea floor and, as far as we know, none of these has included *in situ* seabed gamma spectrometry. Bastin¹ towed a gamma ray detector across recent sediments off the Belgian coast and was able to delineate areas of muds, sands and clays. Summerhayes *et al.*², in the course of a study of phosphorite deposits off NW Africa, also made total gamma measurements at a number of sampling stations upon the continental shelf and slope. Subsequent analysis of the samples showed that anomalous radioactivity could be related to the phosphate content of the sediments. Almost all other seabed radioactivity measurements have been connected with the use of radioactive tracers to determine sediment movement.

We have used a towed seabed gamma spectrometer³ to produce continuous profiles of the natural radioactivity of rocks and sediments on the sea floor. Total count, potassium, "uranium" and "thorium" measurements were made to investigate the possibility of using this technique to map the solid and drift geology. The seabed instrumentation comprises a 76×76 mm NaI(Tl) scintillation detector and EHT unit shock mounted in a 127 mm diameter stainless steel probe. This is attached to 850 m of double-armoured coaxial cable, the lowest 25 m of which is enclosed in a flexible hose of the same diameter as the probe to minimize the risk of snagging on seabed obstacles. The complete unit or "eel" is designed to be towed in contact with the sea floor at speeds of 3–4 kt in depths of up to 200 m.

The shipboard installation is based on Harwell 2000 series electronics with four channels whose energy limits in the present measurements were >0.05 MeV (total), 1.3–1.6 MeV (K), 1.65–1.95 MeV (U) and 2.3–3.3 MeV (Th). Channel outputs were recorded in both analogue and digital form, the energy calibration being maintained by monitoring the 1.46 MeV ⁴⁰K peak with a 100 channel analyser.

Preliminary sea trials of the spectrometer were carried out on MV Surveyor (NERC charter) around northern Britain between August and October 1971 and included a traverse along the 30 fathom line off the Yorkshire coast (Fig. 1). This commenced 11 km east of Flamborough Head

and continued in a NW direction parallel to the shore for a distance of about 80 km to the vicinity of Whitby. The traverse was undertaken to test the "eel" upon a moderately uneven rock bottom and to determine whether the radiometric profile would reflect the known lithology of the sea floor.

The solid and drift geology of the area has been described by Dingle^{4,5}, who has shown that near the coast Triassic to Cretaceous sedimentary formations are well exposed and gently folded into a series of domes and basins. The present traverse crossed two of these structures, the Scarborough Dome and Mallard Basin (see Fig. 1), with the result that the Jurassic succession between the Lower Lias and the Corallian is repeated three times along its length.

The total count, "uranium" and "thorium" profiles recorded along the traverse together with the solid geology are given in Fig. 2. The first is a simplified representation of the ratemeter chart recording and the radioelement profiles have been compiled from successive 500 s scaler counts which were accumulated between the consecutively numbered Decca Navigator position fixes taken at 10 min intervals. The Compton scattering contribution to the "uranium" channel from higher energy "thorium" radiation is not known accurately for the seabed geometry, but we have made an approximate correction to the data on the basis of laboratory measurements with a point source.

The three-fold repetition of the stratal succession is clearly mirrored by the radiometry (Fig. 2). The count rate rises from a minimum over the two Middle Jurassic-Corallian outcrops (fix Nos. 187-191, 216-222) to peaks (198, 208-210, 228) near the Middle-Lower Lias boundaries and fluctuates at an intermediate level (199-206) upon the Lower Lias. These variations are consistent with the lithologies traversed. The Middle Jurassic-Corallian beds are composed predominantly of weakly radioactive freshwater sandstones and shales and marine limestones. The very deep troughs at fix Nos. 188 and 216 may be due to these limestones. In contrast, the Lias is formed mainly of relatively strongly radioactive marine shales with limestone bands which

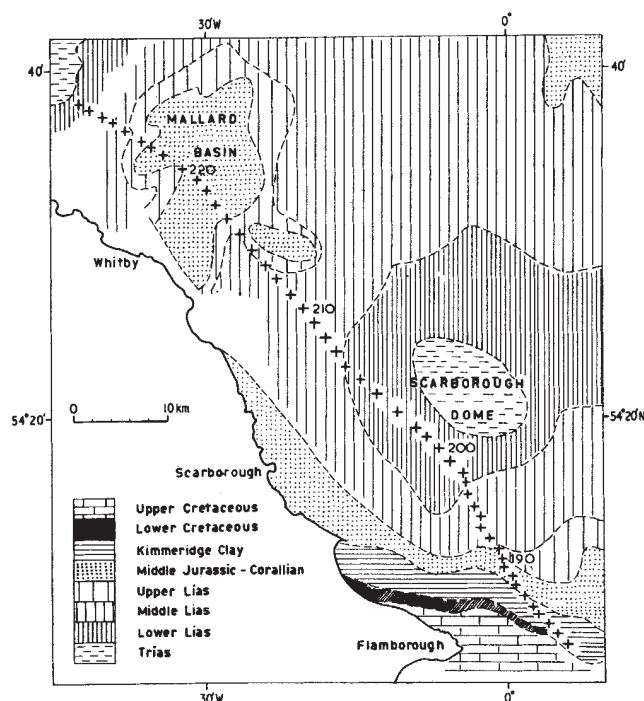


Fig. 1 Plan of Yorkshire coast radiometric traverse. The Decca Navigator position fixes taken at ten minute intervals are marked by crosses. Geology after Dingle⁴.

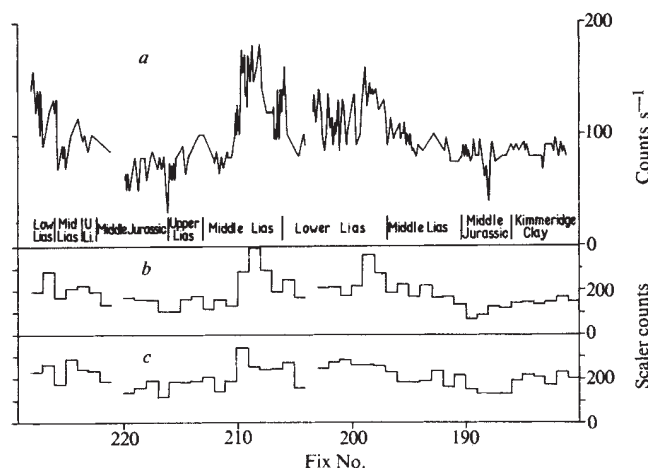


Fig. 2 Total count (a), "uranium" (b) and "thorium" (c) profiles along Yorkshire coast traverse. Each radioelement scaler count was accumulated for 500 s. Middle Jurassic subdivision represents Middle Jurassic-Corallian of Dingle.

increase in number towards the base of the formation. This shale-limestone alternation may account for the large closely spaced fluctuations in the Lower Lias total count record. The radioelement profiles indicate a marked increase of the U:Th ratio at each of the major total count peaks on the Lias and also show a general predominance of thorium over uranium on the Middle Jurassic-Corallian. These relative abundances are characteristic of marine shales and arenaceous deposits respectively.

Although the Jurassic rocks are generally well exposed, Dingle has mapped three drift covered areas along the traverse. The largest of these is a layer of glacial till which completely blankets the Kimmeridge Clay outcrop (181-7) and is presumably responsible for the relatively flat profiles in all three channels. Similar count rates were obtained between fix Nos. 210 and 211 where till overlies Lias shales, and this probably accounts for the abrupt decline in all three channels at this point. The third drift area (216-7) is of sand, which undoubtedly contributes to the very low count rate near fix No. 216.

Although the overall fit between the geology and radiometry is reasonable there are some discrepancies, most notably between the mid-traverse total count peaks and the divisions of the Lias. This could be due partly to the limitations of position fixing as well as to a lack of detailed knowledge of the seabed geological succession.

The geometry of the detector relative to the sea floor is not constant and the channel counts depend in a direct way on the smoothness of the seabed and the depth of the furrow cut by the "eel" as well as on the natural radioactivity of the sediments. Without repeating the measurements along the same traverse it is not possible to be sure that the probe was in contact with the seabed at all times. For example, near fix 216 the count rate is very low and is probably due to an area of sand overlying limestone, but there may have been some loss of contact with the sea floor here also. The gaps in the records at fixes 204 and 221 occur where the "eel" was raised from the seabed to avoid known obstacles.

The detailed evaluation of the pattern of gamma activity and a better understanding of the significance of many of the finer details of these results must await a further and more systematic survey of the area. Similarly a proper analysis of the radioelement channel data requires a careful calibration of the spectrometer on beds of known U, Th and K content. But our results suggest that radiometric techniques offer a valuable new means of extending our knowledge of both the solid and drift geology of the sea floor.

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Radiometric Dating of the Ubeidiya Formation, Jordan Valley, Israel

THE Ubeidiya Formation¹ is known from three localities (Fig. 1) within the Jordan Valley, where it is steeply tilted, faulted and folded^{2,3}. It is rich in prehistoric remains, representing the Developed Oldowan and Early Acheulean⁴. The Ubeidiya Formation is important in the Pleistocene history of the Jordan Valley for two reasons: it is the youngest sedimentary sequence to be severely affected by tectonic movements of the graben, and it contains the oldest human implements ever found in the Middle East.

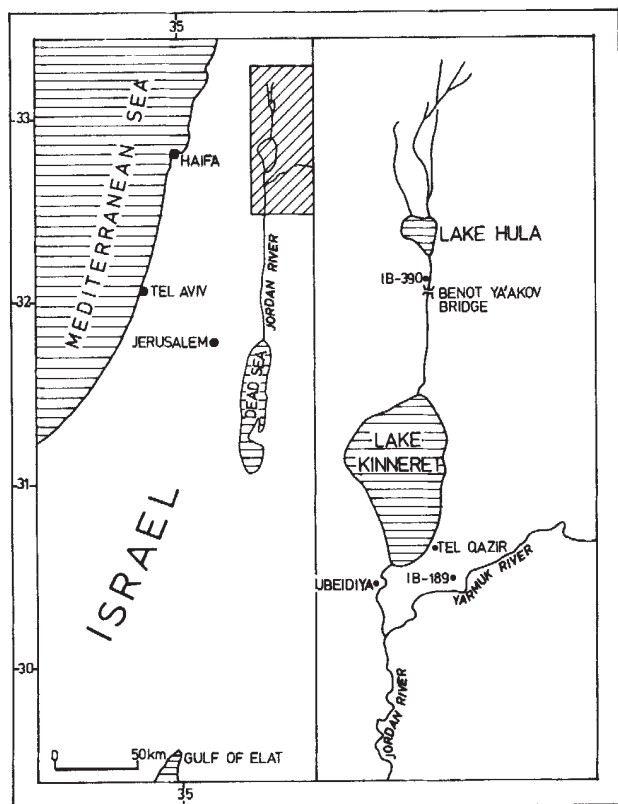


Fig. 1 Location map.

Many inferences concerning the age of the Ubeidiya Formation have been published since it was first described by Blanckenhorn⁵. Blanckenhorn, and later Picard⁶, tended to accept a Pliocene age. Picard², Picard and Baida^{1,7} and Stekelis *et al.*³ regarded the formation as of "Lower Pleistocene or Villafranchian" age, a contention based chiefly on concepts regarding its tectonic position. Horowitz⁸ discussed the possibility of a Middle Pleistocene, approximately Mindel, age of the Ubeidiya Formation, which was also accepted by others⁹⁻¹¹. The assumption of a Mindel age was based principally on palynostratigraphic correlation with deep boreholes drilled in the Dead Sea area¹². ²³⁰Th/U analyses were applied by Bender and Kaufman¹³ in an attempt to determine the age of the Ubeidiya sediments, but no significant results were forthcoming.

The type-section for the Ubeidiya Formation⁷ is described from the vicinity of the site of Ubeidiya (Fig. 1), about 3 km south-west of Lake Kinneret, in the central Jordan Valley. The sequence comprises lacustrine, fluvial and terrestrial sediments, in which two chief cycles have been distinguished, alternating from lacustrine to fluvial conditions.



Fig. 2 Outcrop of Mishmar Hayarden Basalt, from which specimen IB-390 was collected.

Two other outcrops (Fig. 1) were ascribed by Picard⁸ to the Ubeidiya Formation: one comprises a series of tilted freshwater sediments, cropping out near Tel Qazir, to the east of Lake Kinneret, and the other is located near Benot Ya'akov Bridge (*Jisr Banat Yaqub* in Arabic, as was previously described) on the bank of the Jordan River north of Lake Kinneret. The latter outcrop was described in detail by Horowitz¹⁴, who also found a basalt sheet intercalated within the sediments, which were given the local name Mishmar Hayarden Formation. The three outcrops were ascribed by Picard² to the Ubeidiya Formation chiefly because of their structural position—"tilted freshwater series". This assumption was later strengthened by pollen analyses¹⁴, which indicated a great similarity of the pollen spectra in the Benot Ya'akov and Ubeidiya outcrops, and also by the fact that some artefacts turn up in the Benot Ya'akov outcrop. As the number of artefacts is too low, however, it is not possible to make detailed comparisons between them and the rich assemblages of Ubeidiya.

In Ubeidiya itself there are more than ten artefact-containing layers¹⁰ producing different assemblages. These are defined as Developed Oldowan and Early Acheulean, following the terminology of M. D. Leakey^{15,16}. In European terminology these would, apart from one assemblage, correspond to the Abbevillian (=Early Acheulean in African terminology). We have carried out K-Ar measurements on a sample of the Mishmar Hayarden Basalt, collected from the outcrop near Benot Ya'akov Bridge (Fig. 2). The rock, specimen IB-390, is a fresh, massive, non-vesicular olivine basalt.

From the analytical data presented in Table 1, we have calculated an age of $640,000 \pm 120,000$ yr, the error representing analytical uncertainty. Details of analytical methods and constants employed, as well as the regional setting of the Cainozoic basalts of northern Israel, are given in Siedner and Brenner¹⁷.

Table 1 Analytical Data, Calculated Ages and Locations for Dated Basalts from Northern Israel

Specimen and location	K (wt %)	Rad ⁴⁰ Ar ml. 10 ⁻⁶ STP per g	Rad ⁴⁰ Ar Total ⁴⁰ Ar (%)	Calculated age $\pm$ error (yr)
IB-390. Basalt, near Benot Ya'akov Bridge (elevation +100 m a.s.l.)	0.938	0.0239	0.88	$640,000 \pm 120,000$
IB-189. Basalt, above Yarmuk River (elevation +220 m a.s.l.)	0.709	0.0190	4.9	$680,000 \pm 50,000$

The correlation of the Mishmar Hayarden Basalt with the Yarmuk Basalt, suggested by Horowitz¹⁴ on stratigraphic grounds, is corroborated by their radiometric ages (Table 1). A sample of the latter (specimen IB-189) has yielded an age of $680,000 \pm 50,000$ yr, which coincides, within the limits of experimental error, with that of the former.

A deep borehole, Melech Sedom 1—drilled in the centre of the Dead Sea basin which serves as the ultimate erosion base-level for the Jordan Valley—penetrated about 4 km of Pleistocene sediments. These were analysed palynologically¹², and indicated four or five alternations of pluvial and interpluvial conditions. The upper two are correlated with outcrops of Würmian and Rissian age, whereas the third and possibly the fourth are correlated with the Ubeidiya Formation. The assumption that the Ubeidiya Formation, taking into account its two limnic and fluvial cycles, might have been deposited during Günz and Mindel times, has been discussed by Horowitz⁸. We are not sure, however, whether the lower part was deposited through Günz times. It seems that, at any rate, the upper part of the Ubeidiya Formation was deposited during Mindel times.

The Early Acheulean in East Africa is dated as early as 1.5 m.y., extending to about 0.1 m.y. (ref. 18). There is a time gap of about a million years between the East African Acheulean occurrences and the earliest Abbevillian industries in Western Europe, dated as Mindelian in age. There are several hints that the absolute chronology used in the European literature, in the absence of radiometric datings, is perhaps too low¹⁸. The evidence from Ubeidiya Formation, which dates the Early Acheulean in the Jordan Valley, as probably earlier than Mindel, seems to reveal the antiquity of this culture in Asia.

The dated basalt flow from Benot Ya'akov Bridge is clearly part of the upper section of the Ubeidiya Formation. Its age of 640,000 yr should, therefore, be considered as an approximate minimum age for Mindel times.

As mentioned, the Ubeidiya and Mishmar Hayarden formations were strongly affected by tectonic movements. Rissian sediments, the Benot Ya'akov Formation¹⁴, unconformably overlie the tilted Mishmar Hayarden Formation in the Benot Ya'akov Bridge area. It seems therefore that the tectonic movement which caused the tilting of the Ubeidiya Formation occurred some time within the Mindel-Riss Interpluvial and is younger than 640,000 yr. The use of the terms "pluvial" and "interpluvial" and the application of the alpine names to the local time-stratigraphy are discussed by Horowitz¹⁹ and are adopted here.

Palaeomagnetic analysis of the Mishmar Hayarden basalt, carried out in the field on a number of samples using brunton compass, shows that it cooled under conditions of normal polarity. This coincides well with the radiometric age, corres-

ponding most probably with the Brunhes Normal Epoch that commenced some 700,000 yr ago.

A radiometric dating programme to extend the present preliminary investigation to other Quaternary areas and formations in northern Israel will be commenced shortly.

We thank Professor E. Jaeger and Dr J. C. Hunziker of the Min. Petrographisch Institut, University of Bern, for laboratory facilities made available to one of us (G. S.) for the isotopic analyses. Specimen IB-189 was collected by I. Brenner, Geological Survey of Israel. Facilities for the fieldwork were given by the Israel Academy of Sciences and Humanities, through the Expedition for Study of the Pleistocene of the Central Jordan Valley.

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The Structure of Powdered Quartz

DIFFERENTIAL thermal analysis (d.t.a.) of quartz normally reveals an endothermic peak at 573° C, corresponding to the inversion from low quartz to high quartz. If the quartz is subjected to grinding it is observed that the peak size decreases, both in height and area; this effect is usually attributed to conversion during grinding of quartz to some amorphous or vitreous form of silica, as has been described by Dempster and Ritchie¹.

Using a quartz sand from Chatteris, Cambridgeshire, we have studied the effects of grinding for various periods up to 400 h on the d.t.a. peak at 573° C. Samples were prepared in a vibration mill with a steel chamber; d.t.a. traces were recorded at a heating rate of 10° C min⁻¹. Fig. 1 shows that after 400 h milling the peak has vanished, and by the accepted theory this sample should consist entirely of some amorphous phase of silica. This sample was found, however, to have the X-ray structure characteristic of crystalline quartz. X-ray powder pictures are given in Fig. 2a and b for quartz milled

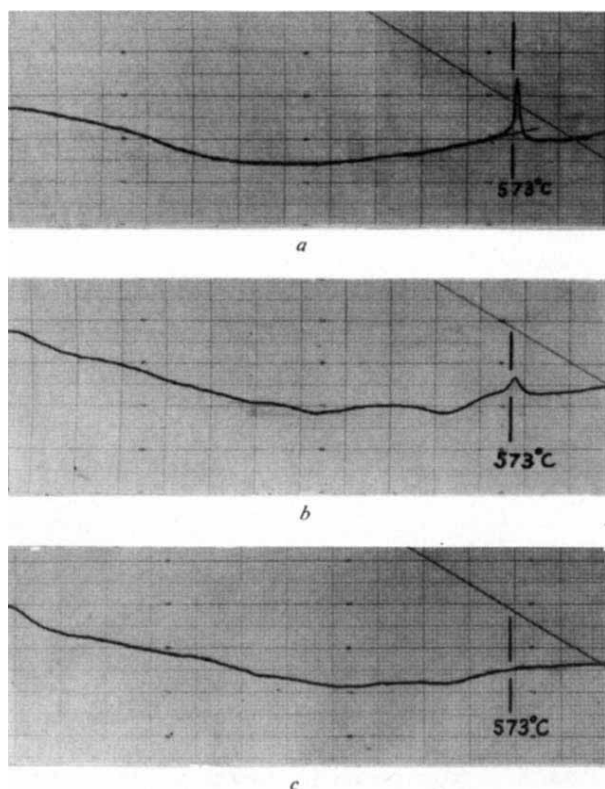


Fig. 1 D.t.a. curves for quartz showing decrease in size of inversion peak at 573°C with milling. *a*, Original quartz sand; *b*, milled 100 h; *c*, milled 400 h.

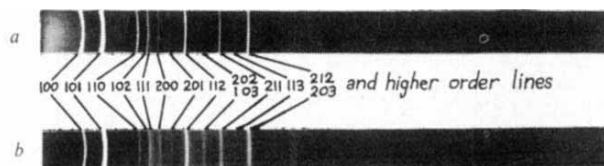


Fig. 2 Debye Scherrer X-ray powder patterns for: *a*, quartz milled 10 h; *b*, quartz milled 400 h, showing that the latter has the structure of crystalline quartz as opposed to an amorphous material. (CuK α radiation, Ni filter.)

10 h and 400 h respectively, and the former may be regarded for purposes of comparison as a reference picture of quartz. The intensities of the low angle diffraction lines revealed that the quartz milled for 400 h consisted of at least 75% crystalline quartz, the diffuse nature of the higher angle lines being a well known effect of either crystal strain or small particle size. In addition, these samples of powdered quartz were found to contain up to 4% by weight of H₂O, absorbed from the atmosphere during milling (Fig. 3).

That water is absorbed by quartz during grinding was reported as early as 1908 by Hillebrand². He ground quartz for 3 h in an agate-mortar and found that the loosely held moisture (liberated below 105°C) increased from zero to 0.35% and the firmly held water (liberated above 105°C) increased from 0.06 to 0.45% by weight. This important work of Hillebrand appears to have been overlooked by recent investigators in this field of research.

Impurities introduced from the steel chamber and balls during milling may affect the experiment in several ways. First, iron oxides increase the affinity of silica for water and might have caused the absorption of the large quantities of H₂O during milling. Second, Keith and Tuttle³ attributed variations in the temperatures of inversion and sluggishness of inversion of specimens of quartz from different sources to the solid solution of impurities in trace amounts: thus the

impurities introduced by milling might have accounted for the decrease in size of the d.t.a. inversion peak.

Another technique of grinding resulting in a different impurity contamination was therefore employed. Electronic grade Brazilian quartz was milled for a period of 500 h in a small agate-mill. The resulting sample evolved 5% by weight of H₂O on heating to 800°C, and did not exhibit the d.t.a. inversion peak characteristic of quartz. Thus the absorption of water vapour and disappearance of d.t.a. inversion peak appeared independent of impurity. To check if the ability to invert at 573°C to high quartz had been suppressed, this material was examined in a Lenne camera, which gives a continuous record of X-ray structure versus temperature. Lenne diagrams for Brazilian quartz agate-milled 5 h (reference material) and Brazilian quartz agate-milled 500 h are shown in Fig. 4*a* and *b* respectively.

Both diagrams are very similar. There is a gradual change of slope of the diffraction lines owing to thermal expansion of the samples: lines labelled "Pt" are due to the platinum specimen holder. At 573°C there is a sudden discontinuity of the lines owing to the 0.86% volume expansion which accompanies inversion from low quartz to high quartz, which appears less sharp for the quartz milled 500 h. Also the III line was absent for both samples above 573°C, which is further evidence that both samples change from low to high quartz. Thus although the quantity of quartz detectable by d.t.a. becomes less during grinding, it is apparent that the resultant product still has the structure of low quartz which changes to high quartz when heated through 573°C.

Thermal conductivities of the samples were measured by Lee's disk method for samples packed to the same degree as for the d.t.a. (Fig. 5), and were found approximately independent of milling after the first few hours. The decrease in size of the d.t.a. peak is therefore not due to changes of thermal conductivity.

We determined the densities of samples withdrawn from the steel vibration mill using specific gravity bottles and water as the working fluid (Table 1). Two corrections were made: first, for absorbed H₂O (making the assumption that the absorbed H₂O effectively has the same density as liquid water at the same temperatures); second, for the presence of iron contaminant (measured by flame spectroscopy and by hydrogen displacement from acid). The average of the corrected values comes to 2.650 ± 0.012 g ml.⁻¹, close to the value for quartz which is 2.650 g ml.⁻¹ at 25°C. Therefore it appears that the observed changes in the measured density were adequately

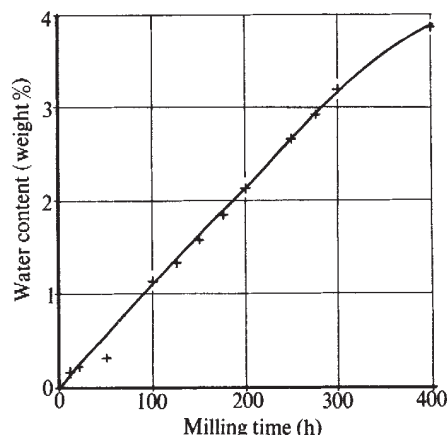


Fig. 3 Relation between water content of powdered quartz and duration of milling. The water contents were determined from the loss of weight on heating to 800°C, checking that the loss in weight was equal to the quantity of water condensable from the evolved vapours. Although samples could be heated to constant weight at lower temperatures they retained a certain fraction of absorbed H₂O which could only be driven off by heating to 800°C.

Table 1 Density Results for Powdered Quartz at 25° C

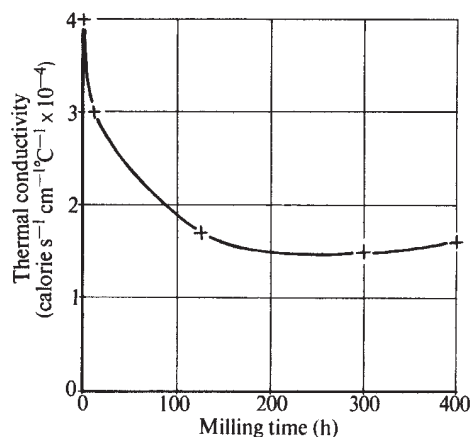
Milling time (h)	Measured density (g ml. ⁻¹)	Density corrected for the presence of moisture only (g ml. ⁻¹)	Density corrected for the presence of water and iron impurity (g ml. ⁻¹)
0	2.643	2.643	2.643
10	2.656	2.663	2.656
20	2.654	2.663	2.650
50	2.649	2.662	2.643
100	2.630	2.680	2.655
125	2.621	2.680	2.655
150	2.606	2.675	2.647
175	2.592	2.673	2.643
200	2.577	2.669	2.638
250	2.574	2.691	2.658
275	2.559	2.686	2.651
300	2.543	2.680	2.644
400	2.540	2.710	2.678

Density of quartz at 25° C = 2.650 g ml.⁻¹ Mean = 2.650 g ml.⁻¹
s.d. = ± 0.012 g ml.⁻¹

explained in terms of the absorbed H₂O and iron introduced during milling.

It is important to note the drying procedure used by those investigators who have reported falls in density of quartz during powdering. Ray⁴ employed a temperature of 150° C and found the density of a silver sand to fall from 2.638 to 2.528 g ml.⁻¹ during milling; he concluded that as much as 25.7% of the quartz had been converted into vitreous silica. This agreed well with a value which he obtained from the heats of solution. Sosman and Merwin⁵, however, repeated Ray's work, but optical examination revealed that the powdered quartz was still completely crystalline.

Dale⁶ pointed out that Ray had not taken into account contamination by agate during milling. He found that although the density of quartz decreased during grinding, part of the fall could be accounted for by such contamination

**Fig. 5** Thermal conductivity data for powdered quartz.

(density of agate ~2.60 g ml.⁻¹). If, however, the remaining reduction of density was due to the conversion of the quartz to vitreous silica (2.2 g ml.⁻¹), then this amounted to only a few per cent as compared with Ray's 25.7%. Dale employed a temperature of 200° C for drying his samples.

Our finding that heating at 800° C is necessary to drive off all the water from the samples of quartz suggests that the drying temperatures of 150° C and 200° C reported above were inadequate and the samples would have contained some H₂O still in combination.

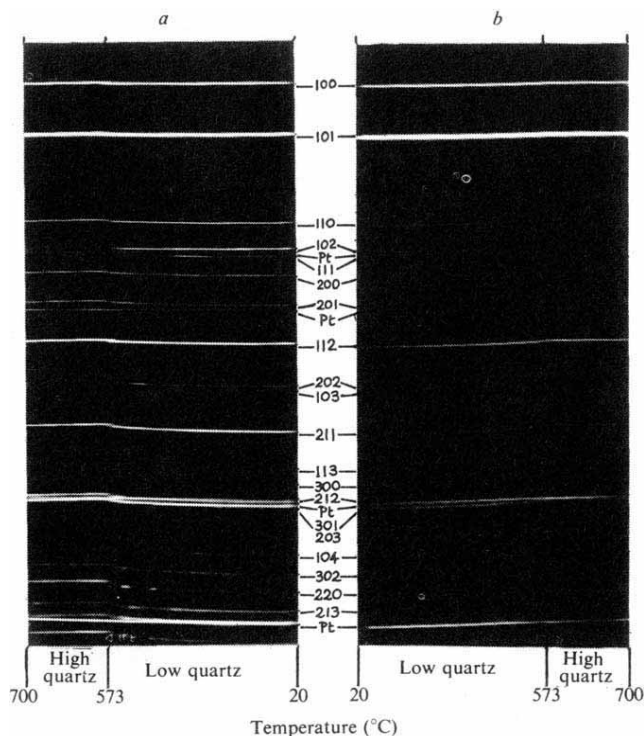
Clelland and Ritchie⁷ found an increased initial solubility and decreased density for quartz when powdered. They rejected hydration as an obvious possibility, because of differences in the solubility characteristics between powdered quartz and silica gels. They concluded that the surfaces of the quartz particles had become converted to "vitreous silica of the Beilby type produced by melting and surface flow". Dempster and Ritchie⁸ also found a reduction in density after grinding, but not as large as that reported by Clelland and Ritchie. They attributed this partly to the effects of impurities and partly to the "more rigorous drying of the dusts before weighing (110° C, 4 h)"; again, our results suggest that their drying procedure was inadequate.

Sakabe⁹, using a drying temperature of 150° C, found that the longer the quartz was ground, the more intense were the OH infrared absorption bands. Also, Soda¹⁰ concluded that the silanol group exists in the surface structure of powdered quartz.

Thus there is considerable evidence that quartz absorbs atmospheric moisture during powdering, but it does not appear to have been pointed out that this is the most probable reason for the decrease in density of quartz produced by milling.

Further research suggests that the disappearance of the d.t.a. inversion peak at 573° C with milling is due to a spreading of the inversion over a small range of temperature. When d.t.a. is carried out at about twice the normal heating rate, at 18° C/min, the "lost" d.t.a. peak again becomes quite pronounced, possibly because the effect of a dispersion of the inversion over a small range of temperature becomes less and a greater fluctuation of differential temperature is produced. When d.t.a. is carried out at low rates of heating, each fragment of quartz inverts at its own individual inversion temperature, and more time is available for heat to be conducted to the sample as a whole, giving rise to a smaller inversion peak.

It would appear that when quartz is powdered, it acquires properties which would classify it as a "microform". According to Sosman¹¹, fine subdivision and twinning may so alter the properties of a phase of silica that it can no longer be readily identified, even when it forms the basis of an aggregate. Sosman has called them the "microforms" of silica, and their obscurity is almost entirely due to their fine grain size. Sosman has classified the microforms of silica into microcrystalline,

**Fig. 4** Lenne diagrams of milled quartz. *a*, Quartz milled 5 h; *b*, quartz milled 500 h. Lenne pictures give plot of X-ray structure against temperature. The inversion of the quartz milled 500 h appears less sharp than the inversion of the quartz milled for 5 h.

microamorphous, and microaphanitic, and further on a geometric basis into microgranular, microlamellar, and microfibrillar. More recently, Kloss¹² reported that, unlike macrocrystalline quartz crystals, microcrystalline quartz crystals generally show no sharp inversion point, and the inversion takes place over an interval of nearly 50° C. Our work suggests that it is best to describe the product of powdering quartz as microcrystalline quartz, which has an X-ray structure corresponding to quartz but is not normally detectable by d.t.a. unless carried out at high heating rates. In addition, this microcrystalline quartz contains chemisorbed H₂O.

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Image Formation by Induced Local Interactions: Examples Employing Nuclear Magnetic Resonance

AN image of an object may be defined as a graphical representation of the spatial distribution of one or more of its properties. Image formation usually requires that the object interact with a matter or radiation field characterized by a wavelength comparable to or smaller than the smallest features to be distinguished, so that the region of interaction may be restricted and a resolved image generated.

This limitation on the wavelength of the field may be removed, and a new class of image generated, by taking advantage of induced local interactions. In the presence of a second field that restricts the interaction of the object with the first field to a limited region, the resolution becomes independent of wavelength, and is instead a function of the ratio of the normal width of the interaction to the shift produced by a gradient in the second field. Because the interaction may be regarded as a coupling of the two fields by the object, I propose that image formation by this technique be known as zeugmatography, from the Greek ζευγμα, "that which is used for joining".

The nature of the technique may be clarified by describing two simple examples. Nuclear magnetic resonance (NMR) zeugmatography was performed with 60 MHz (5 m) radiation and a static magnetic field gradient corresponding, for proton resonance, to about 700 Hz cm⁻¹. The test object consisted of two 1 mm inside diameter thin-walled glass capillaries of H₂O attached to the inside wall of a 4.2 mm inside diameter glass tube of D₂O. In the first experiment, both capillaries contained pure water. The proton resonance line width, in the absence of the transverse field gradient, was about 5 Hz.

Assuming uniform signal strength across the region within the transmitter-receiver coil, the signal in the presence of a field gradient represents a one-dimensional projection of the H₂O content of the object, integrated over planes perpendicular to the gradient direction, as a function of the gradient coordinate (Fig. 1). One method of constructing a two-dimensional projected image of the object, as represented by its H₂O content, is to combine several projections, obtained by rotating the object about an axis perpendicular to the gradient direction (or, as in Fig. 1, rotating the gradient about the object), using one of the available methods for reconstruction of objects from their projections¹⁻⁵. Fig. 2 was generated by an algorithm, similar to that of Gordon and Herman⁴, applied to four projections, spaced as in Fig. 1, so as to construct a 20 × 20 image matrix. The representation shown was produced by shading within contours interpolated between the matrix points, and clearly reveals the locations and dimensions of the two columns of H₂O. In the second experiment, one capillary contained pure H₂O, and the other contained a 0.19 mM solution of MnSO₄ in H₂O. At low radio-frequency power (about 0.2 mW) the two capillaries gave nearly identical images in the

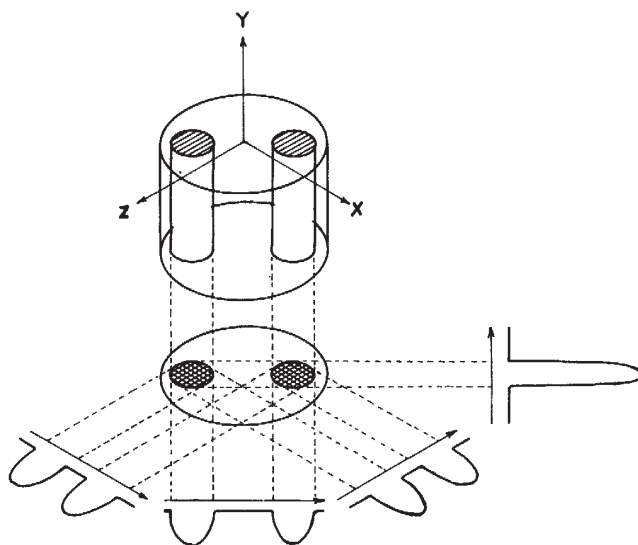


Fig. 1 Relationship between a three-dimensional object, its two-dimensional projection along the Y-axis, and four one-dimensional projections at 45° intervals in the XZ-plane. The arrows indicate the gradient directions.



Fig. 2 Proton nuclear magnetic resonance zeugmatogram of the object described in the text, using four relative orientations of object and gradients as diagrammed in Fig. 1.

zeugmatogram (Fig. 3a). At a higher power level (about 1.6 mGauss), the pure water sample gave much more saturated signals than the sample whose spin-lattice relaxation time T_1 had been shortened by the addition of the paramagnetic Mn^{2+} ions, and its zeugmatographic image vanished at the contour level used in Fig. 3b. The sample region with long T_1 may be selectively emphasized (Fig. 3c) by constructing a difference zeugmatogram from those taken at different radio-frequency powers.

Applications of this technique to the study of various inhomogeneous objects, not necessarily restricted in size to those commonly studied by magnetic resonance spectroscopy, may be anticipated. The experiments outlined above demonstrate the ability of the technique to generate pictures of the distributions of stable isotopes, such as H and D, within an object. In the second experiment, relative intensities in an image were made to depend upon relative nuclear relaxation times. The variations in water contents and proton relaxation times among biological tissues should permit the generation, with field gradients large compared to internal magnetic inhomogeneities, of useful zeugmatographic images from the rather sharp water resonances of organisms, selectively picturing the various soft structures and tissues. A possible application of considerable interest at this time would be to the *in vivo* study of malignant tumours, which have been shown to give proton nuclear magnetic resonance signals with much longer water spin-lattice relaxation times than those in the corresponding normal tissues⁶.

The basic zeugmatographic principle may be employed in many different ways, using a scanning technique, as described above, or transient methods. Variations on the experiment, to be described later, permit the generation of two- or three-dimensional images displaying chemical compositions, diffusion coefficients and other properties of objects measurable by spectroscopic techniques. Although applications employing nuclear magnetic resonance in liquid or liquid-like systems are simple and attractive because of the ease with which field gradients large enough to shift the narrow resonances by many

line widths may be generated, NMR zeugmatography of solids, electron spin resonance zeugmatography, and analogous experiments in other regions of the spectrum should also be possible. Zeugmatographic techniques should find many useful applications in studies of the internal structures, states, and compositions of microscopic objects.

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BIOLOGICAL SCIENCES

Island Lizards: the Genetic-Phenetic Variation Correlation

NATURAL populations of many organisms are known to contain much more genetic variation than would have been predicted by all but a minority¹ of geneticists two decades ago. Individuals of several species have up to 22% of their loci heterozygous, and from 0–50% or more of the loci in a population are polymorphic, although the higher estimates may result from sampling error^{2–4}; vertebrates tend to be at the lower end of these ranges. Estimates such as these are based on electrophoretically detectable variation in proteins, so the true levels of genetic variation are probably higher⁵. These generalizations are gaining wide acceptance, but there is still some unease about their accuracy. The fundamental question is whether the loci being sampled are representative of the genome as a whole. We here present evidence that the electrophoretic approach is relatively unbiased.

Two groups of lizards were used: eight species of *Anolis* from the West Indies and thirteen populations of the side-blotched lizards *Uta stansburiana*, *sensu lato*, from California and Mexico, caught in 1971 and 1972. Geographic variation is not a source of heterogeneity, as all specimens from a locality were collected within a few hundred metres of one another. After capture, they were transported alive or on dry ice to the laboratory and stored at -76°C until needed. After skinning, water-soluble proteins were routinely extracted and electrophoresed⁶. Six of the eight *Anolis* species were from Puerto Rico, and two, *A. extremus* and *A. roquet*, were from Barbados and Martinique, respectively.

A single morphological character was used to estimate morphological variation in the *Anolis* species; the number of subdigital scales on the longest toe (second) on the hind foot, starting with the most distal lamella and counting proximally. Variability in this character is correlated with variability in other scale characters, but the other characters were not scored as accurately. Estimates of genetic variation in the *Anolis* species were derived from the starch-gel electrophoresis patterns of enzymes and nonenzymatic proteins, which together appear to represent the gene products of twenty-one or twenty-two loci. The proteins assayed were lactate dehydrogenases, malate dehydrogenases, α -glycerol-phosphate dehydrogenase, isocitrate dehydrogenases, indophenol oxidase, phosphoglucose isomerase, phosphoglutamate, glutamic oxaloacetate

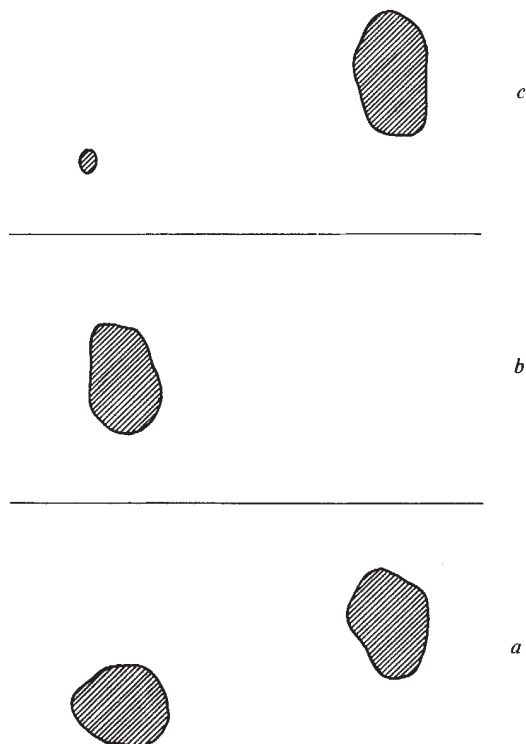


Fig. 3 Proton nuclear magnetic resonance zeugmatograms of an object containing regions with different relaxation times. a, Low power; b, high power; c, difference between a and b.

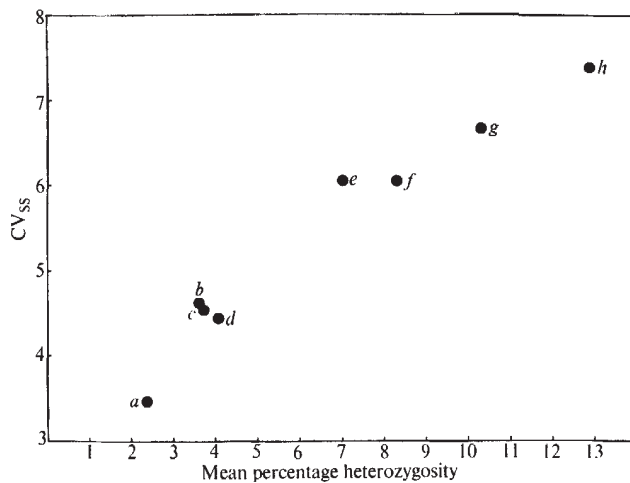


Fig. 1 The association in eight species of *Anolis* of the coefficient of variation of subdigital scales (CV_{ss}) and mean percentage of loci for which an individual was found to be heterozygous in a population. a, *A. stratulus*; b, *A. poncensis*; c, *A. extremus*; d, *A. roquet*; e, *A. evermanni*; f, *A. gundlachi*; g, *A. krugi*; h, *A. pulchellus*. Sample sizes range between 21 and 30.

transaminases, 6-phosphogluconic dehydrogenase, 4 general proteins, fumarase, peptidase, xanthine dehydrogenase and, except in *A. roquet*, alcohol dehydrogenase. Esterases were excluded because of difficulty in their interpretation.

Five external characters were the basis for estimates of morphological variation in *Uta*. The characters, as described elsewhere⁷, include mid-dorsal scales (24), right circumorbitals (28), right supraoculars (31), right femoral pores (34), and scale organs (42) on 31. Except for characters 28 and 31, none are significantly correlated. We used the mean of the five coefficients of variation⁸ to estimate overall morphological variation in a population. Estimates of genetic variation were derived from the starch-gel electrophoresis patterns of ten enzymes and four nonenzymatic proteins, which together seem to represent the gene products of nineteen loci. The proteins were the same as with *Anolis* with the following exceptions: two esterases were scored but fumarase, peptidase, xanthine dehydrogenase and alcohol dehydrogenase were not screened.

A priori, the two kinds of variation afford different views of the genome. The morphological data probably provide information on variation over a relatively large fraction of the genome, but environmental heterogeneity may also contribute significantly to the variances of these characters. The electrophoretic data, on the other hand, provide information on a very small fraction of the genome, but this information is virtually free of nongenetic effects. Significant correlation between these two operationally independent estimates would support the hypothesis that both are accurately estimating the same thing—overall genetic variation. It would then follow that a sample of loci as small as twenty or twenty-five can give a reliable estimate of genetic variation in a population. On the other hand, such a correlation does not necessarily imply any overlap in the genetic bases of the morphological and protein characters.

Fig. 1 shows the relation between the two presumed estimates of genetic variation among the eight *Anolis* species. The statistical significance of the association is obvious. Three species available to us were not included because sexual dimorphism in the scale count artificially inflated the coefficient of variation, and the samples were too small to segregate by sex.

Fig. 2 shows the same relation among the *Uta* populations. The pattern of association demonstrates a significant correlation (Spearman rank correlation is 0.60, $P < 0.05$) when considering only populations on the more isolated islands beyond the 100 m depth contour. Most of these deep-water populations

are phenetically distinct and have probably been in continuous existence since before the last glacial maximum⁹. In general, the populations on the mainland and on near-shore, shallow water islands do not conform to the above pattern, being more variable morphologically for a given level of estimated protein variability. We do not know why this is, but one possibility is that these populations have large environmental contributions to their variances compared to the deep-water populations.

Elsewhere⁸ (and in preparation), we discuss the separate question of the possible genetic and ecological causes of the different levels of genetic-phenetic variation on islands.

Marshall and Allard¹⁰ have shown a correlation in variation between two sets of Mendelian characters in grasses of the genus *Avena*; one set was electrophoretic, the other was morphological. Our results extend the correlation to continuously varying, obviously polygenic characters. We believe that the available evidence supports the hypothesis that the enzymes and other structural proteins that we and others are using to estimate genetic variation are, in fact, a representative sample of gene products. Our data, however, also suggest that other factors, perhaps environmental heterogeneity, may be a very important source of variation in some morphological characters. In this regard, the correlation in Fig. 1 is somewhat higher than anticipated. It can easily be shown that estimates of heterozygosity based on only twenty loci have appreciable standard errors, so it is likely that further studies will produce results more like those in Fig. 2.

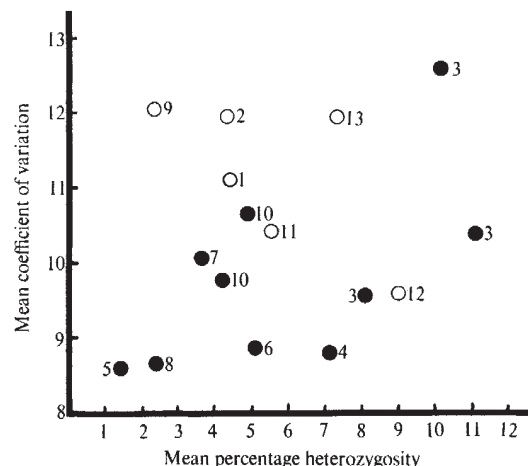


Fig. 2 The association in *Uta stansburiana* of morphological variation, $\bar{V}$ (see text), and average (= mean) % of loci for which an individual was found to be heterozygous in a population. The numbers refer to the following localities: 1, UCSD campus; 2, Punta Bunda, Baja California; 3, three sites on Angel de la Guarda Island; 4, Partida Norte Island; 5, Salsipuedes Island; 6, North San Lorenzo Island; 7, South San Lorenzo Island; 8, San Pedro Martir Island; 9, San Ildefonso Island; 10, two sites on Carmen Island; 11, San Jose Island; 12, San Francisco Island; 13, Espiritu Santo Island. Sample sizes range between 18 and 35. Open circles signify shallow water and mainland populations.

Also, we conclude that, if general heterozygosity is an important source of the differences in morphological variability among the populations, then the assumption that electrophoretically detected allozymes are of no selective significance^{11,12} is weakened unless, of course, it is assumed that morphological variation has no selective significance. Several articles indicate that stabilizing selection, at least, affects morphological variation¹³⁻¹⁵.

We have considered alternative explanations of the observed correlations. Perhaps the most reasonable is that local environmental diversity determines both genetic variability and morphological variability, but by separate paths. The

available data do not support this conclusion⁸, but genetic studies will be required to rule it out altogether.

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Relationship of Enzyme Polymorphism to Species Diversity

SUCCESSFUL adaption by a species to a particular portion of diverse environment depends not only upon the physical characteristics of that environment, but also upon the reliability with which a particular set of characteristics is encountered. A high degree of specialization might be more advantageous when environmental factors occur predictably than when they do not.

Slobodkin and Sanders¹ have suggested that regions of high species diversity tend to be characterized by high environmental predictability. A similar hypothesis was advanced by Connell and Orias². Little unambiguous empirical evidence exists on this point. Hessler and Sanders³ have shown that deep oceans have high species diversity compared with estuaries, which is consistent with this hypothesis.

A second hypothesis concerns amounts of genetic variation. Species occupying niches, the characteristics of which are highly predictable, might be expected to maintain a lesser degree of genetic variation than species occupying less reliable niches, while situations of low environmental predictability might tend to promote polymorphic gene variation^{4,5}. Again, this point has not been empirically demonstrated.

These two untested hypotheses, both phrased in terms of environmental predictability, imply that environments of high predictability may be accompanied not only by high species diversity but also by low degrees of polymorphic gene variation. Thus the two hypotheses are compatible only if levels of species diversity are inversely related to the extent of polymorphic gene variation.

There are few data on which to base a comparison of species diversity and gene polymorphism. The recently reported study on enzyme polymorphism in the Hawaiian *Drosophila* by Rockwood *et al.*⁶ does permit such a comparison, although it must be considered preliminary (the data involve the use of but one standard, interspecific homologies are uncertain, and the sample sizes are often small, particularly from Kauai where some species are represented by single individuals).

The levels of *Drosophila* species diversity on each of the Hawaiian Islands, and the evolutionary relationships between these species, are well documented (for a review see Carson⁷). I here express the levels of *Drosophila* species diversity on each island in terms of the total number of *Drosophila* species per island; species diversity may also be expressed solely in terms of the "picture wing" species (Maui=30, Hawaii=17, Oahu=11, Kauai=9). Following other authors, I treat the islands of Maui, Molokai, and Lanai as a single evolutionary unit (the three islands have been fused into a single above-water land mass at least twice, and are in close proximity).

To estimate the level of allozyme diversity characteristic of each island, I have utilized the Rockwood data on patterns of enzyme polymorphic variation at six enzyme loci among fifty-one "picture wing" species of Hawaiian *Drosophila*. This estimation involves several assumptions which must be carefully examined. (a) It assumes that the selection of species examined is representative of the total number of species. The almost exclusively island-endemic "picture wing" species group of Hawaiian *Drosophila* is distributed in a manner similar to that of the total number of *Drosophila* species (15 to 20% of all species are members of the picture wing group on each of the islands). (b) It assumes that the number of allelic forms observed in the sample is representative of the species, rather than reflecting the character of a local population. In the few species in which the effect of geographic isolation has been examined, differences are chiefly in gene frequency rather than in the total number of allelic forms observed. (c) It assumes an unbiased selection of alleles. All populations considered must be analysed for the same assortment of loci, as some loci will exhibit far more diversity than others. Among the fifty-one picture wing species, thirty-eight species were analysed at all six loci, nine species at five loci, and one species at four loci; the remaining three species were analysed at fewer loci, and were not considered in my analysis.

I have expressed levels of allozyme diversity as the ratio of the number of different allozyme types observed to the number of species examined. Similar results are obtained if allozyme diversity is expressed as $(\sum n \log n)/(\text{the number of species examined})$, where n =the proportion of observed species in which a given allele occurs.

Comparing the estimates of allozyme and species diversity described above, it is clear that an inverse relationship exists (Fig. 1). Similar results are obtained when information theory measures of allozyme diversity are used, or when species diversity is characterized solely in terms of the picture wing species.

These levels of allozyme diversity do not correlate with obvious physical and genetic factors, such as: (1) the age of the islands (Kauai is the oldest, Hawaii the youngest); (2) the area of the island (Kauai is the smallest, Hawaii the largest); (3) the distances between them; (4) estimates of evolutionary distance (the chromosomal relationships among the Hawaiian *Drosophila* are known in detail⁷; among the picture wing species, assuming the ancestral form to be *D. primaeva*, no significant regression exists for allozyme diversity as a function of the number of inversion differences from ancestral form); (5) founder effects (chromosomal relationships indicate that the minimum number of inter-island founders in the picture wing species is one for Kauai, six for Oahu, six for Maui, and nine for Hawaii); (6) sample size (the small samples are from Kauai, which shows the

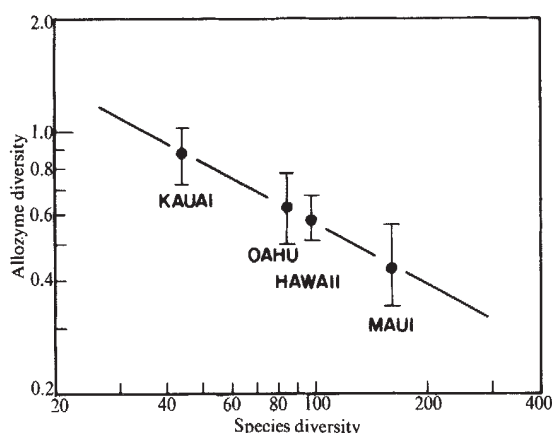


Fig. 1 The relation of allozyme diversity to species diversity in Hawaiian *Drosophila*. Allozyme diversity is expressed as the number of different allozyme types of an enzyme observed on an island divided by the number of species examined on that island. The allozyme data used are those of Rockwood *et al.*⁶. Species diversity is expressed as the total number of *Drosophila* species found on a given island. Mean values for the six enzyme loci are presented, with standard error indicated. A linear plot is also highly significant. A linear regression (calculated using UCIA Biomed. Multiple Regression Program) yields a regression coefficient of -0.004 ; $F_{1,22} = 6.68$, $0.01 < P < 0.025$, indicating a high level of significance.

greatest diversity; increasing these sample sizes could not reduce the number of allozyme types seen); (7) total number of allozyme types (the greatest number of different types are seen on Maui, the least on Kauai).

A further technical point must be considered. As inter-specific homologies are not certain in the Rockwood study, it is important to estimate the extent to which possible errors in allele assignment might affect the significance of the allozyme diversity estimates of Fig. 1. Such mistaken assignments would occur most frequently between alleles of similar mobility. Thus errors in allele assignment should reflect the frequency distribution of the allele mobility types on the various islands. In the Rockwood study, the shapes of the allele distribution curves are very similar for a given locus from island to island. For the four islands, mean values for "evenness"⁸ of allele distributions are 0.46, 0.51, 0.53, and 0.49, indicating that the relative information content of the allele distributions is quite similar on the four islands. Thus errors in allele assignment should not affect the significance of the relationship seen in Fig. 1.

The inverse relationship observed between species diversity and enzyme polymorphism diversity is that which would be expected if both parameters were influenced by environmental predictability, as current hypotheses suggest. As detailed knowledge of the ecology of specific species becomes available, and more complete survey data are obtained on the relevant allozymes, it may become possible to relate niche breadth with respect to a particular resource to the levels of allozyme diversity at loci concerned with utilization of that resource. Until such data are available, however, it should be kept clearly in mind that measures of diversity which average over a variety of enzymes or over ecologically diverse species are at best only an indication of more complex underlying processes.

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Carcino-Foetal Human Liver Ferritins

FERRITIN is an iron-storage protein found in the cytoplasm of a wide variety of plant and animal cells^{1,2}. Structurally, the molecule comprises a hollow protein shell, apoferritin, composed of 20 or 24 subunits, within which variable amounts of inorganic iron may be sequestered. These subunits may not be chemically identical since multiple molecular forms of differing charge, isoferritins, have been found in several organs by electrophoresis^{3,4} or electrofocusing^{5,6}. Although the structural relationship of the isoferritins is unclear, these findings raise the possibility that the charge differences may represent primary structures coded by different genes. In addition to the isoferritins found in normal cells, an "abnormal" ferritin has also been found in malignant cell lines⁷ and in livers of tumour bearing animals^{8,9}. As part of our investigations into tumour specific and embryonic antigens, we have examined the isoferritin profile in human hepatoma and compared it to that found in normal adult and foetal liver. Here we supply evidence for a unique isoferritin species in human hepatoma that is not present in normal adult liver. This tumour-specific isoferritin may correspond to a similar isoferritin found in foetal liver in early gestation.

Ferritin was isolated from normal human livers, foetal livers at various stages of gestation and from human hepatoma tissue by the method of Drysdale and Munro¹⁰. A chromatographic step on CM-cellulose was omitted to prevent possible loss of isoferritins of differing charge. Tissues were blotted dry of residual blood, homogenized in 4 volumes of water, then heated to 75° F for 2 min to precipitate heat labile proteins. The supernatant fraction was adjusted to pH 4.6 to remove other contaminants and ferritin was subsequently recovered from the supernatant and precipitated in 33% ammonium sulphate. The pellet was dissolved in 0.02 M KH₂PO₄, chromatographed on 'Sephadex G-200' and eluted in the void volume. These preparations contained only ferritin and its higher polymeric forms when examined by polyacrylamide gel electrophoresis.

Table 1 pI of Human Liver Ferritins

Peak	Normal	Foetal	Hepatoma
1	5.55		
2	5.50		
3	5.45*	5.45	5.47
4	5.33	5.34*	5.36
5	5.29	5.28	5.29*
6		5.22	5.23*
7			5.15

* The principal molecular form.

As a further purification, some of these preparations were subjected to isoelectric focusing in a 110 ml. sucrose density gradient containing 4% (w/v) 4-6 or 5-7 'Ampholines' (LKB Produkter, Sweden¹¹). After 3-5 days electrolysis, 0.5 ml. fractions were collected from the bottom of the column, and the pH gradient measured with a microelectrode. Apoferritin

was identified and quantitated by electroimmunodiffusion¹² using monospecific rabbit anti-human liver ferritin.

All preparations resolved into multiple components on isoelectric focusing, with at least six or seven distinguishable peaks. The *pI*s of the isoferritin peaks in hepatoma, adult and foetal liver are given in Table 1. The principal peak in normal adult liver was isoelectric at *pH* 5.45 with several minor components between *pH* 5.3 and 5.5. The foetal and hepatoma isoferritin profiles showed the same components, but in both cases the more acidic components predominated. In addition to these common components, the hepatoma ferritin contained a more acidic form, *pI* 5.1, that was not demonstrated in normal liver.

To examine these profiles in more detail, the purified ferritin preparations were subjected to gel electrofocusing¹³ (Fig. 1). Normal ferritin consistently showed at least three major bands. The hepatoma isoferritins contained at least one of these three components, but in addition demonstrated a molecular form with a lower *pI* that is not present in normal ferritin. This tumour-specific isoferritin was also apparent in early foetal ferritins, 12–20 weeks of gestation, which contained bands common to both hepatoma and normal ferritin with a variable pattern. The oldest foetus (35 weeks of gestation) had an isoferritin pattern that was indistinguishable from normal, adult ferritin.

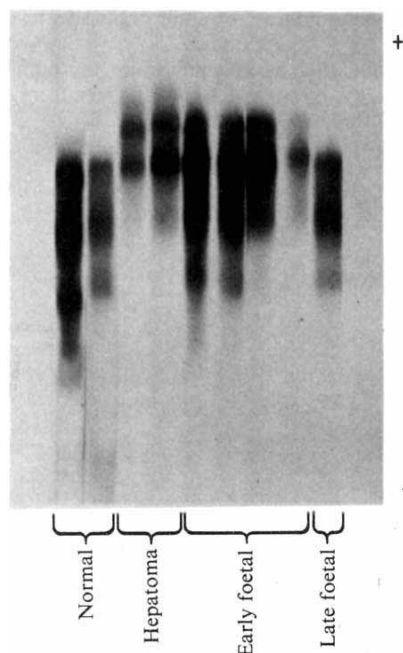


Fig. 1 Analytic isoelectric focusing in 4% polyacrylamide gels using 2% ampholyte *pH* range 4–6. Ferritin isolated from two normal, two hepatoma and five foetal livers was applied. After equilibrium was attained, the gels were stained for iron with Prussian blue. Similar patterns were obtained by using protein stains.

In order to confirm that these multiple forms of ferritin represented distinct molecular species, the isoferritins were separated and re-examined. The acidic, central and basic isoferritin fractions from hepatoma ferritin were separated by preparative isoelectric focusing in sucrose. The portions were dialysed against 0.02 M phosphate buffer *pH* 7.4 and concentrated by vacuum dialysis. The concentrated pools were then refocused on the analytical 4% polyacrylamide gels as previously described and stained for iron with Prussian blue (see Fig. 2). The different molecular forms of hepatoma ferritin did not redistribute, but refocused to the same position. The isoferritin isolated with the most acid *pI* was not present in normal ferritin, suggesting the presence of a chemically unique hepa-

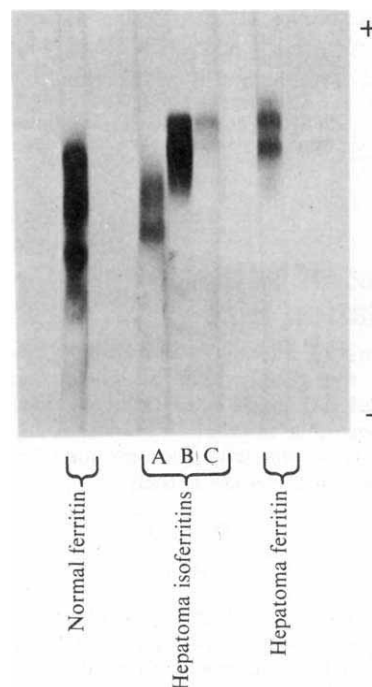


Fig. 2 Hepatoma isoferritins were separated by preparative isoelectric focusing into a basic pool (A), *pI* 5.32–5.80, the main peak (B), *pI* 5.20–5.30, and the most acidic forms (C), *pI* 4.74–5.18. These pools were dialysed against 0.02 M phosphate buffer (*pH* 7.4), concentrated, and aliquots applied to analytic isoelectric focusing in 4% polyacrylamide gels, ampholyte *pH* 4–6. After equilibrium was attained, the gels were fixed and stained for iron by Prussian blue.

toma ferritin form. The structural relationships of the isoferritins revealed by isoelectric focusing have not yet been resolved. The heterogeneity is not due to difference in iron content or aggregate size and appears to represent charge differences either from different primary structure or post-synthetic modification of one or more of the subunits. The appearance of a unique hepatoma isoferritin suggests that the tumour not only synthesizes at least some of the components found in normal ferritin, but may make a unique tumour-specific or carcino-foetal ferritin subunit. The biochemical structure of these ferritin forms and their subunit structure are under further investigation.

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The Effect of Mutation on Population Size

AFTER the work of Haldane¹ and Muller², much has been written about the genetic load caused by mutation. This mutational load had been defined as the fraction by which the mean fitness of a population subject to mutation differs from the fitness of the wild (non-mutant) genotype³. The operational definition of load is then

$$L = \frac{W_{\max} - \bar{W}}{W_{\max}} \quad (1)$$

where $W_{\max}$ is the fitness of the non-mutant genotype, and $\bar{W}$ the mean fitness of the population subject to mutation.

Some workers have supposed, implicitly or explicitly, that the average selective value is necessarily an indicator of the relative fitness or competitive ability of a population compared to other populations. This supposition is incorrect because it is based on an extrapolation of measures of relative fitness within populations (selective values) to comparisons between populations^{4,5}. Further confusion has been caused by the assumption that the genetic load is a measure of factors directly related to population size⁶. Here I report some results from a study of the effects of mutation on population numbers, using earlier work on density-dependent selection⁷⁻¹¹ to bridge the gap between the theories of ecology and population genetics.

The proportional reduction of numbers brought about by mutation (the numerical load) for populations that are in numerical equilibrium can be defined in an analogous way to the definition of the conventional genetic load.

$$NL = \frac{\hat{N}_0 - \hat{N}_{\text{mut}}}{\hat{N}_0}$$

where $\hat{N}_0$ is the numerical equilibrium in the absence of mutation, and $\hat{N}_{\text{mut}}$ is the equilibrium in its presence¹¹.

Assuming a large random-mating population with discrete generations and without immigration or emigration, let us suppose that there are two alleles M and m at an autosomal locus, and that M is completely dominant to m. The frequency of M among the adults of one generation is p , and the frequency of m is q ($p+q=1$). M is the "wild-type" gene and m is the mutant. The mutation rate from M to m is μ . When m is rare we can ignore back-mutation from m to M. If mutation occurs during the formation of gametes and if all three genotypes have equal fertility, the gene frequency of m among the gametes will be

$$q' = q + \mu(1-q)$$

When the phenotypes have different probabilities of surviving to produce offspring, represented by the selective values a (for M-) and c (for mm), the phenotype frequencies after selection will be

Phenotype frequencies after selection	M-	mm
	$a(1-q'^2)$	cq'^2

and the overall change of gene frequency will be

$$\Delta q = \frac{(1-q')[q'^2(c-a) + a\mu]}{(1-\mu)[q'^2(c-a) + a]} \quad (2)$$

When there is a balance between mutation and selection, Δq is zero and

$$\hat{q}' = \sqrt{\frac{a\mu}{a-c}}$$

where $\hat{q}'$ is the non-trivial equilibrium value of q' .

From equation (1) the genetic load at equilibrium is

$$L = \frac{a - [q'^2(c-a) + a]}{a} = \mu \quad (3)$$

The selective values (a and c) are conventionally defined as measures only of relative fitness. The equations given above, however, are equally valid if a and c are absolute fitnesses. In this event they measure changes in the numbers of each genotype from generation to generation. The average selective value ($\bar{W} = q'^2(c-a) + a$) is then related to the overall change in numbers (ΔN) by

$$\Delta N = N(\bar{W} - 1) \quad (4)$$

where N is the total number of adult organisms in the population.

When the population is at equilibrium for both numbers and gene frequency, $\Delta q = 0$ and $\Delta N = 0$. Then, from equations (2) and (4),

$$a = \frac{1}{1-\mu} \quad (5)$$

$$c = \frac{\hat{q}'^2 - \mu}{\hat{q}'^2(1-\mu)} \quad (6)$$

These equations are general, and can be applied whether the selective values are constant or variable. If the selective values are functions of population size, equations (5) and (6) can be used to derive the value of N at equilibrium. Thus we can solve $\hat{N}$ as well as $\hat{q}'$. The precise result will depend upon the form of the relation between selective value and population size.

Following an earlier study¹¹, this relation is assumed to be

$$a = \frac{w_1 k_1}{k_1 + w_1 N(1-q'^2) + \alpha_1 w_2 N q'^2} \quad (7)$$

$$c = \frac{w_2 k_2}{k_2 + w_2 N q'^2 + \alpha_2 w_1 N(1-q'^2)} \quad (8)$$

where w_1 and w_2 represent the "intrinsic selective values" (density-independent rates of increase, including the effects of density-independent mortality, which is assumed to act first), k_1 and k_2 measure the "carrying capacity" of the environment for each genotype, and α_1 and α_2 are coefficients of competition.

A consideration of a and c makes it clear that a mutant could be disadvantageous in three different ways. It could have a reduced intrinsic selective value (w), a reduced carrying capacity (k), or a reduced competitive ability (either an increased value of α_2 or a reduced value of α_1).

These three situations can be considered separately. If the mutant has a reduced intrinsic selective value, we can assume $w_1 = w$, $w_2 = w(1-s)$. $k_1 = k_2$, $\alpha_1 = \alpha_2 = 1$ (note that if α_1 and α_2 are less than one the system may become a balanced polymorphism¹¹). Substituting in equations (7), (8), (5), (6) and (2) we find the numerical load

$$NL_{(w)} = \frac{\mu}{(w-1)(1-\mu)} \quad (9)$$

Similarly, the numerical load for a mutant reducing the carrying capacity (if $k_1 = k$, $k_2 = k(1-s)$, $w_1 = w_2$, $\alpha_1 = \alpha_2 = 1$) is

$$NL_{(k)} = \frac{w\mu}{w-1} \quad (10)$$

When mutation increases α_2 (that is, when $\alpha_1 = 1$, $\alpha_2 = 1+s$)

$$NL_{(\alpha_2)} = \frac{w\mu}{w-1} \text{ as before} \quad (11)$$

but when it decreases α_1 (that is, when $\alpha_1 = 1-s$, $\alpha_2 = 1$)

$$NL_{(\alpha_1)} \approx \frac{w - \sqrt{s\mu w(w-1)}}{w-1 - \sqrt{s\mu w(w-1)}} \quad (12)$$

which is negative if $s > \mu$ (that is, when there is a balance between mutation and selection). Details of the approximation are given elsewhere¹².

If the density-dependent component of selection is assumed to act before the density-independent component, the numerical loads are unchanged, except that the w load becomes

$$\frac{w\mu}{(w-1)(1-\mu)}$$

like the k and α_2 loads.

Several conclusions emerge. First, it is possible to combine the theoretical assumptions of ecology and population genetics, and to predict the effects of mutation on equilibrium population size. Second, although all disadvantageous mutants produce the same genetic load (as conventionally defined), different types of mutants may have different effects on the numerical equilibrium. Third, in relation to their effects on population size, disadvantageous mutants can be grouped into three broad classes, which are not mutually exclusive; w -mutants, with reduced density-independent selective value (and consequently a reduced intrinsic rate of increase), k -mutants, with a reduced carrying capacity, and α -mutants with a reduced competitive ability. Selection against α -mutants probably corresponds to the "soft selection" of Wallace⁶. Fourth (perhaps the most surprising conclusion), in some circumstances the presence of disadvantageous mutants can cause an increase in population size, despite the fact that the mutants are eliminated by natural selection.

Studies using other ecological models, including the logistic conclusion, suggest that these conclusions are general (see ref. 12 and L. Nunney, personal communication). It is quite clear that in order fully to understand the consequences of mutation we must take into account its effects on the ecological parameters of populations.

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Effect of Hyperbaric Oxygen on Cultured Foetal Hearts

FOETAL mouse hearts and foetal hearts from other species have been shown to have remarkably consistent performance in organ culture. Wildenthal^{1,2} demonstrated that various substances added to an organ culture medium prolonged the survival of foetal hearts, and Hughes and Longmore³ showed that survival time and beating were related to the stage of development of the embryo, the younger hearts living and beating longer and better than the older hearts. Longmore and Hughes⁴ have shown that there is no difference in the performances of composite hearts made from parts of foetal hearts of different species at the same stage of maturity. It has been suggested by Wildenthal (personal communication) that the effect of substances on the heart may be different before and after the nerve end plates have developed.

All the culture techniques used 95% oxygen and 5% CO₂ at 1 atm but New⁵ has shown that hyperbaric oxygen, at 2 to 3 atm, permits prolonged survival of twenty-five somite rat embryos in static culture medium and forty somite rat embryos in circulating medium. The inference was that hyperbaric oxygen might improve the performance of standard foetal heart cultures. From our clinical experience on the effects of hyperbaric oxygen we doubted whether oxygen at above normal pressures would have anything but harmful effects. To establish whether this was so, we set out to culture, in our standard medium, control hearts and hearts set up in a simple hyperbaric chamber.

Litters of mice, 11 and 16 days of gestation, were used. Half of each group were used as controls and half were subjected

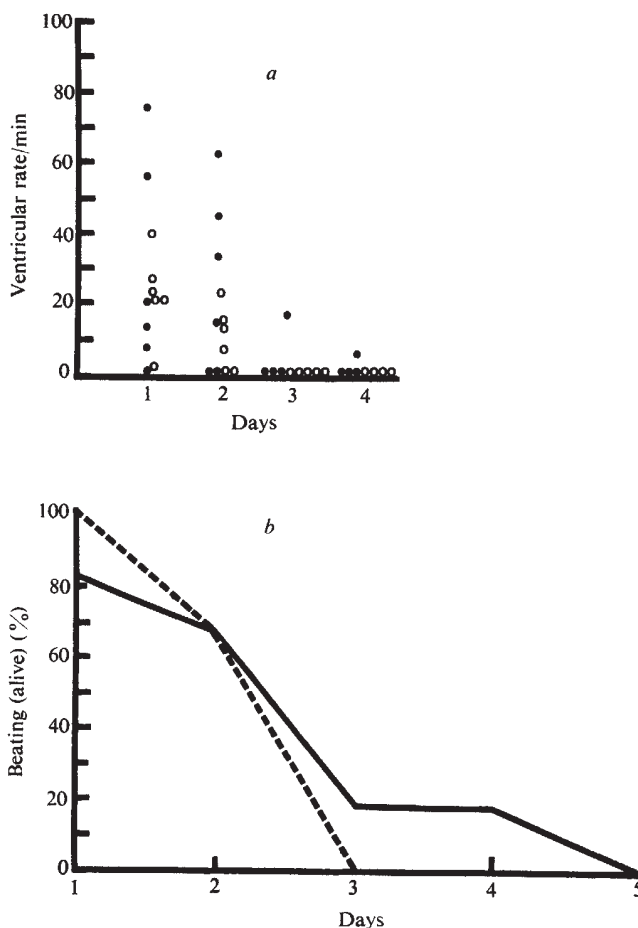


Fig. 1 Eleven-day-old foetal hearts (before innervation). a, Beating performance. ●, Control; ○, hyperbaric. b, Survival. —, Control; ---, hyperbaric.

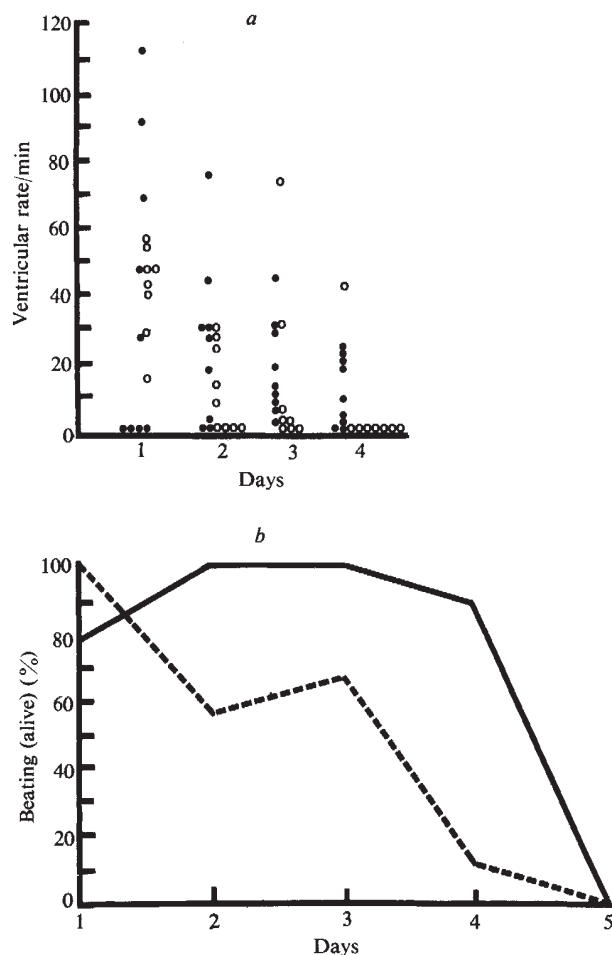


Fig. 2 Sixteen-day-old foetal hearts (after innervation). *a*, Beat-ing performance. ●, Control; ○, hyperbaric. *b*, Survival. —, Control; ---, hyperbaric.

to hyperbaric oxygen. During dissection the atria were left intact whenever possible. The hearts were placed on stainless steel wire mesh grids and arranged so that just the bottom surface of the hearts was in direct contact with the medium. Burroughs Wellcome 199 culture medium, with 35% colostrum deprived calf serum, plus 50 mg ml⁻¹ insulin and 0.1 µg ml⁻¹ cortisol, was used as the culture medium.

A special chamber was constructed for the hyperbaric cultures in order to maintain and withstand the increased pressure. Inlet and outlet valves, as well as a pressure gauge, were added to regulate the pressure to precisely two atmospheres. The culturing technique was exactly as for the controls except for the increased P_{O_2} . The P_{CO_2} remained at 38 mm mercury for both groups while the P_{O_2} was increased from 722 mm of mercury to 1,482 mm of mercury in the hyperbaric groups.

Both the control hearts and those in the hyperbaric chamber were examined daily to check rate and strength of contractions. The medium was changed every second day. Hearts were considered to be living as long as there was any sign of contraction. For the hyperbaric group approximately 15 min was allowed for decompression before examination to prevent any remote possibility of dissolved oxygen coming out of solution as destructive bubbles.

In all the experiments, which were satisfactory from the technical point of view, the control hearts lived longer and beat faster than the hearts which were subjected to hyperbaric oxygen (Figs. 1 and 2). An anomaly has been that although the hyperbaric hearts beat more slowly and died sooner than the controls, the strength of their contraction was observed to be greater during the short time that they lived. The total

number of these stronger beats was reduced by merit of their shorter survival and of their slower rate.

The detrimental effect of hyperbaric oxygen can probably be related to the small size of the cultured organs and the fact that they rested on the surface of the medium rather than being immersed in it. Hearts cultured and used for the evaluation of drugs should therefore not be cultured in hyperbaric oxygen.

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The Effect of Fatty Acids on the Binding of Tryptophan to Plasma Protein

THE amino-acid tryptophan has a special role as a precursor of the putative transmitter 5-hydroxytryptamine (5HT). Furthermore, in the brain, tryptophan hydroxylase, the rate-limiting enzyme for 5HT synthesis, is normally unsaturated with tryptophan^{1,2}. Therefore any mechanism by which brain tryptophan concentration can be altered may conceivably be able to influence brain function.

Food deprivation^{3,4} or immobilization stress⁴ both lead to increased brain tryptophan and increased turnover of brain 5HT as indicated by raised concentrations of its metabolite 5-hydroxyindolylacetic acid. The increase of brain tryptophan is not simply due to increased plasma tryptophan as these parameters are not significantly correlated⁴. It is, however, associated with an increase of the small fraction of plasma tryptophan which is free⁵ (ultrafilterable). Also, a number of drugs which when given to rats increase their brain tryptophan also release protein-bound (non-ultrafilterable) tryptophan from plasma *in vitro*⁶. These findings point to plasma-free tryptophan as an important determinant of brain 5HT turnover and in turn raise the question of what controls levels of the former.

Not only the plasma-free tryptophan concentration but also that of unesterified fatty acid increases during deprivation⁵. The possibility therefore arises of a causal relationship between these changes. This is also suggested by the finding that oleate interfered "to a minor extent" with the binding of tryptophan to bovine serum albumin, albeit under non-physiological conditions⁷. Plasma unesterified fatty acids are normally almost completely bound to albumin^{7,8} while plasma tryptophan is largely bound to albumin⁷.

It has now been shown that the addition *in vitro* of physiologically occurring unesterified fatty acids to rat and human plasma within the range of physiological concentration results in elevation of free tryptophan. Linoleic, oleic and palmitic acids were used. These are the major unesterified fatty acids of human plasma⁹ and similar results were obtained on rat plasma when analysed by a gas chromatographic method.

Human and rat blood samples were collected into heparinized tubes, immediately centrifuged and the plasma deep

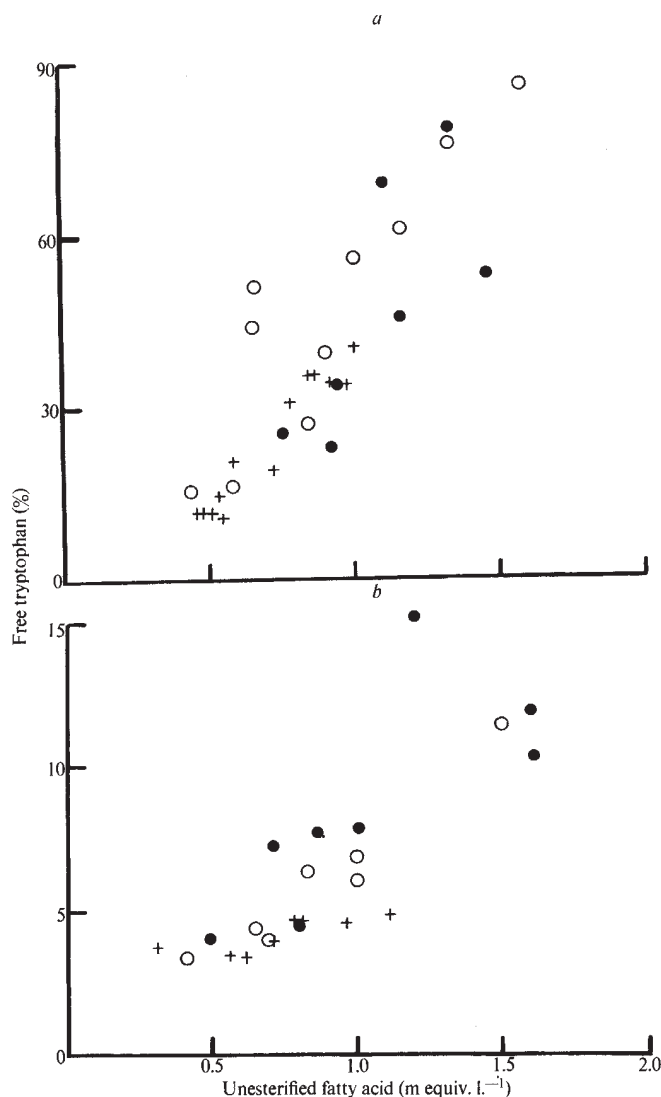


Fig. 1 Effect of *in vitro* addition of unesterified fatty acids to plasma on free (ultrafilterable) tryptophan. *a*, Rat plasma; *b*, human plasma. $\circ$, Linoleic acid; $\bullet$, oleic acid; +, palmitic acid. Correlations: free tryptophan versus unesterified fatty acid. Rat: linoleic (10), $r=0.90$, $P<0.001$; oleic (7), $r=0.73$, $P\approx 0.05$; palmitic (13), $r=0.95$, $P<0.001$. Human: linoleic (7), $r=0.97$, $P<0.001$; oleic (8), $r=0.74$, $P<0.05$; palmitic (8), $r=0.79$, $P<0.05$. Number of observations in parentheses. One batch of bulked rat plasma (total tryptophan = $12.1 \mu\text{g ml}^{-1}$) was used with palmitic acid and a second batch (total tryptophan = $16.2 \mu\text{g ml}^{-1}$) with linoleic and oleic acids. A single batch of bulked human plasma was used (total tryptophan = $14.3 \mu\text{g ml}^{-1}$).

frozen, except for 0.05 ml. of each human plasma on which unesterified fatty acid was determined¹⁰. Human plasmas with fatty acid >0.6 mequiv. l^{-1} were discarded and the rest bulked. All rat plasmas were bulked. Fatty acids were dissolved in samples of bulked plasmas by a modification of the method of Meinertz¹¹. Briefly, 0.25–2.0 ml. of 2.0 mM solutions of the fatty acids in petroleum ether (40° – 60° C) were pipetted into 18 mm diameter tubes and made to 2.0 ml. with petroleum ether. The solutions were taken to dryness at 37° C on an 'Evapomix' multiple evaporator. After addition of 2.0 ml. pooled plasma/tube the dried fatty acids were partly dissolved by gentle shaking at 37° C for 1 h, the supernatants were pipetted off and free and bound tryptophan and fatty acid determined on them as previously described⁵ (Fig. 1). Increase of free tryptophan correlated significantly with the amount of fatty acid dissolved for all three fatty acids and for both rat and human plasma. Total tryptophan concentrations were comparable for both rat and human plasmas but free tryptophan concentrations in the absence of added fatty acid were considerably greater in rat plasma. An increase of the fatty acid concentration from 0.5 to 1.0 mequiv. l^{-1} led to four-fold and almost two-fold increases of the free tryptophan concentrations of rat and human plasma respectively. In a subsidiary experiment (not shown in Fig. 1) *in vitro* increase of human plasma palmitic acid to a total unesterified fatty acid concentration of 2.0 mequiv. l^{-1} led to 50% of the total tryptophan being free.

Previously the best indication that increased plasma unesterified fatty acid led to increased free tryptophan was that, after heparin injection, both were elevated⁵. Heparin releases tissue lipase into the plasma so that plasma glycerides are hydrolysed to unesterified fatty acids¹². It was conceivable that heparin influenced tryptophan binding by some mechanism involving not fatty acids but increased sympathetic activity¹³. We now find, however, that previous administration of the sympathetic β -blocker propranolol did not prevent the increases of plasma fatty acid or free tryptophan after heparin injection (Table 1). On the contrary, results suggest that propranolol increases the effect of heparin on tryptophan.

Results obtained therefore strongly indicate that plasma fatty acid changes have a role in determining the availability of tryptophan to the brain and hence 5HT turnover therein. They also suggest a mechanism by which the many hormonal agents which alter lipolysis and fatty acid levels through influencing fat cell cyclic AMP¹⁵ might be able to alter brain 5HT turnover. Such a mechanism could be significant in many physiological or pathological circumstances. Also the alteration of fat cell cyclic AMP concentration by drugs might perhaps also lead to altered brain 5HT turnover. Finally, raised plasma unesterified fatty acid concentrations in conditions such as liver disease¹⁶ and migraine related to fasting¹⁷ suggest the possibility of increased brain 5HT turnover in these conditions.

We thank the Medical Research Council and the Research

Table 1 Effect of Heparin and Propranolol on Plasma Total and Free Tryptophan and Plasma Unesterified Fatty Acids

0 min	Treatment	30 min	Total ($\mu\text{g ml}^{-1}$)	Tryptophan Free ($\mu\text{g ml}^{-1}$)	% Free	Unesterified fatty acids (mequiv. l^{-1})
Saline	Saline		17.68 ± 3.77	$P<0.02$	9.6	$P<0.001$
Saline	Heparin		14.53 ± 3.47		19.9	
Propranolol	Saline		19.32 ± 3.12	$P<0.01$	10.0	$P<0.02$
Propranolol	Heparin		19.55 ± 3.01		32.8	
						$\left\{ \begin{array}{l} 0.20 \pm 0.07 \\ 0.62 \pm 0.15 \end{array} \right.$ $\left\{ \begin{array}{l} 0.27 \pm 0.15 \\ 0.66 \pm 0.27 \end{array} \right.$

Injectations were made by tail vein with the exception of the propranolol (1 mg kg^{-1}) and saline injections at 0 min. These were made as divided injections, half by tail vein and half intraperitoneally following the procedure of Akerblom, Martin and Cingolani¹⁴. Heparin dosage was $5,000 \text{ IU kg}^{-1}$. Blood was collected at 45 min. Each group contained 6 rats. Results given as means ± 1 s.d.

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The Use of Phospholipid Film for Shaping Cell Cultures

It would be useful for many studies of cell-cell interaction (for example, contact inhibition of movement, topoinhibition, electrical coupling) to be able to prepare cell cultures of various defined shapes and sizes. This can be done by protecting the whole surface of the culture substrate, except for desired regions, with a non-adhesive substance. The cells would then adhere and proliferate only in these regions. The protective substance must be (i) non-adhesive for cells; (ii) non-toxic for cells; (iii) insoluble in the media and (iv) strongly attached to the underlying substrate so that neither the size nor shape of adhesive region would change during cultivation. Lieberman *et al.*¹ used dried agar film on a collagen layer as the non-adhesive substance for cardiac muscle cells.

Our aim was to find a non-adhesive film, suitable for experiments with fibroblasts and other types of cultured cells. A number of substances were tried (paraffin, fatty acids, cholesterol) and found to be unsuitable as they were all more or less adhesive for mouse fibroblasts. The only film which satisfied our requirements outlined above was that prepared from brain phospholipids.

The lipids were extracted from the white matter of calf brain by chloroform-methanol^{2,3}. They were dried before use and redissolved in decane or benzene to a concentration of 10 mg ml.⁻¹. To obtain the film, a drop (about 0.02 cm³) of the solution was drawn out of the pipette into the middle of the coverslip, which was rotated horizontally at 2–2,500 r.p.m. This spread the lipids evenly and, after drying, a film was formed strongly attached to the coverslip. A part of this film could be easily removed (mechanically or with a solvent) so that regions of clean glass of any shape could be made. In particular very narrow strips (5–15 μ m wide) could be cleaned

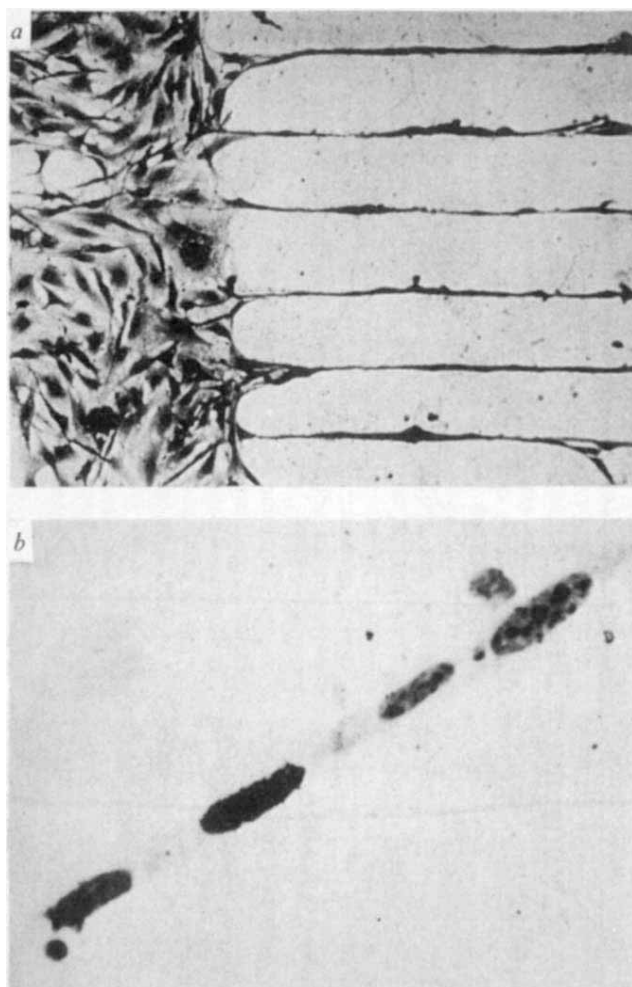


Fig. 1 Mouse embryo fibroblasts growing on the strips from the lipid film. *a*, Cells migrated into the strips from the monolayer ($\times 70$). *b*, Autoradiographic preparation of the cells in the strips labelled with ³H-thymidine (1 μ Ci ml.⁻¹ for 2 h) ($\times 280$).

with a blade or with a thin tungsten electrode. The lipid film was found to be firmly attached to the glass: the width of the strips, scratched in the film, did not change after 7 days of incubation in the serum supplied medium, either with the cells or without them.

The following cell types were used: (i) mouse embryo fibroblasts; (ii) the cells of L-strain⁴; (iii) "Chim" strain cells obtained from mouse sarcoma induced by plastic film, and (iv) epithelial kidney cells, transformed with SV40. Cultivation media, the methods of autoradiography and time-lapse microcinematography were similar to those described earlier^{5,6}.

The cells of all the types used did not spread on the lipid film. As shown by time-lapse cinematography the cells lying on the lipid film retained their spherical form for many hours and continuously formed and withdrew short cytoplasmic processes. These cells remained alive for at least 3 days; they could be reseeded on the glass after that period. When only a part of the glass was covered by the lipid film the cells normally attached themselves to the glass even in the immediate vicinity of the lipid layer. The fibroblasts near the film eventually oriented themselves parallel to its edge. The leading edge of the cell contacting with the edge of the film did not stop undulating, but did not attach to phospholipid. Simultaneously a new leading edge was developed usually in the direction of the border of the film. The cells in contact with the edge of the lipid layer were able to synthesize DNA as well as other cells on the glass; for example, the ³H-thymidine labelled mouse fibroblasts growing for 4 days in narrow

(15 μ m wide) strips (Fig. 1) of the glass, surrounded by lipid film had the same labelling index as the control cells on the clean coverslip.

All these experiments confirm that the lipid film was stable, non-adhesive and non-toxic for the culture types used.

By removing a certain part of the lipid film it is possible to obtain the culture of almost any desired shape. In particular, the cells growing on narrow (10 μ m wide) strips of the glass may be used for many types of experiments. The cells in these strips formed "monolines", that is, rows of elongated cells (Fig. 1b). Directed cell migration could be easily examined in these strips; half the coverslip was cleaned of the lipid before seeding the cells and several days later, after a confluent monolayer was formed on the glass, the strips were scratched in the film and the cells began to migrate in this narrow region.

It is not clear what characteristic of the surface of the lipid film is essential for its nonadhesiveness. Adhesion of cells to various substrates seems to be relatively independent of their hydrophobic or hydrophilic properties⁷. Electro-negativity of the surface of phospholipid film may play an important role⁸. Possibly the interaction of the cell surface with that of artificial phospholipid membrane may be considered as a simplified model of cell membrane to cell membrane interaction. In this connexion it would be useful to study cell interactions with films made of various types of lipids.

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Cycloheximide affects Memory within Minutes after the Onset of Training

WHEN mice are given brief discrimination training in a T-maze following intracerebral or subcutaneous administration of the protein synthesis inhibitors cycloheximide or acetoxycycloheximide, their learning curves are indistinguishable from saline-injected controls^{1,2}. Retention measured 3 h after training is also identical in the drug-treated and control groups, but 6 h after training the drug-treated mice exhibit a striking impairment of retention^{1,2}. These results suggested that cerebral protein synthesis is not required for retention for at least 3 h after training. We now report that using an alternative training procedure a cycloheximide-sensitive component of memory storage can be detected within minutes after the beginning of training. This suggests that in some circumstances cerebral protein synthesis may be required for normal expression of memory within minutes after learning has begun.

We trained mice in the Deutsch carousel³, an automated discrimination training apparatus. Mice were secured by the tail

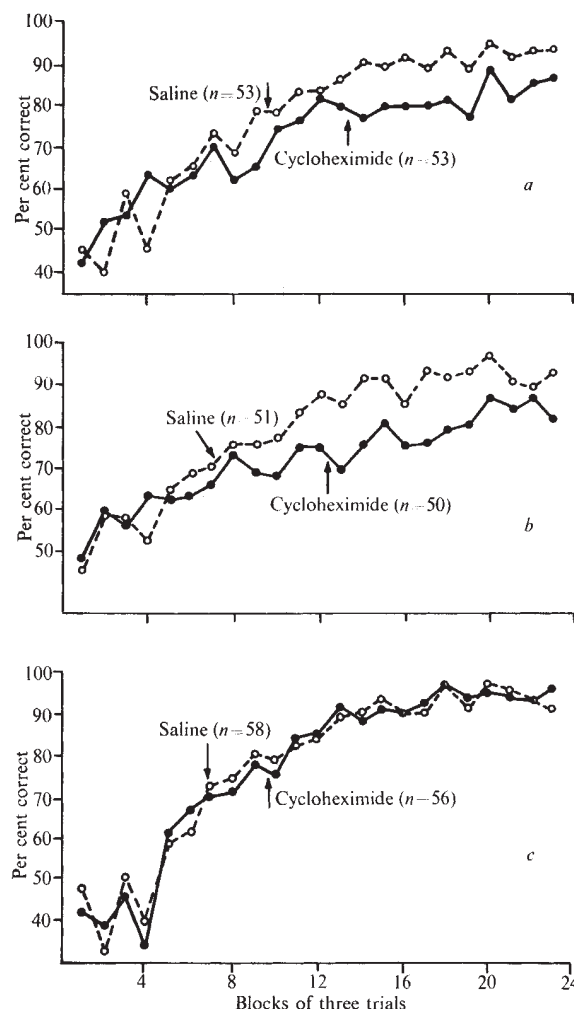


Fig. 1 Mice were trained for sixty-nine trials 10 min (a), 30 min (b) and 210 min (c) after subcutaneous injection of 120 mg/kg cycloheximide or saline. The resulting learning curves of cycloheximide-treated and saline-treated mice were divided into thirds (trials 1–23, 24–46, 47–69) and submitted to a two-way analysis of variance having repeated measures on one factor¹⁰. When cycloheximide was given 30 min or 10 min before training, both the effect of drug treatment (30 min $F=8.0$, 10 min $F=6.3$) and the effect of trials $\times$ drug (30 min $F=10.7$, 10 min $F=7.1$) were significant ($P<0.02$). When cycloheximide was given 210 min before training, neither the effect of drug ($F=0.1$) nor drug $\times$ trials ($F=0.4$) approached significance ($P<0.25$). Individual comparisons¹⁰ indicated that during trials 1–23, the effect of cycloheximide on training did not approach significance in either of the conditions ($P>0.25$). Thus, the effect of cycloheximide given 10 min or 30 min before training is measurable only after twenty-three trials.

in the centre of a circular platform, facing the perimeter, and rotated for each trial to one of three positions. At each position, a mouse could escape shock by touching the smaller of two stainless steel objects. Details of this apparatus and training procedure have been described³. Mice hybridized from Balb/c females and C3H males were injected with 120 mg/kg cycloheximide or saline subcutaneously. Determination⁴ of incorporation of ¹⁴C-leucine into cerebral protein indicated that more than 95% of cerebral protein synthesis was inhibited 10–40 min after injection. When mice were trained for sixty-nine trials beginning 30 min after injection with cycloheximide or saline, their learning curves were not distinguishable for the first fifteen to twenty-five trials (Fig. 1). This observation corroborates our earlier reports that performance during initial training for up to twenty-seven trials in this task is not affected by cycloheximide³ and that initial training in maze tasks, which requires fewer than twenty trials, is also not affected by this drug^{1,2}. However, beyond the first fifteen to twenty-five

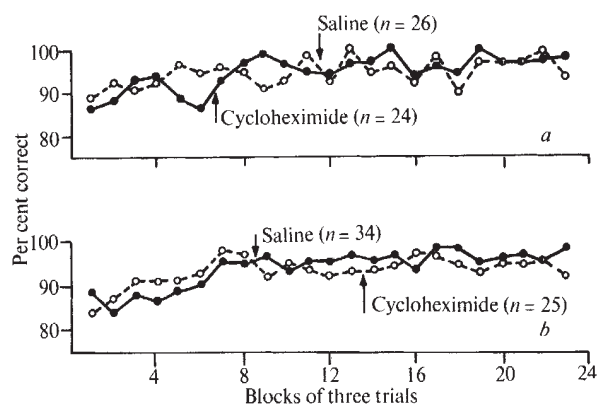


Fig. 2 Mice were trained for sixty-nine trials in the Deutsch carousel and then given a further sixty-nine trials 24 h later. Thirty minutes before retesting (a) or 210 min before retesting (b), mice were given 120 mg/kg cycloheximide or saline subcutaneously. A two-way analysis of variance with repeated measures¹⁰ indicated that neither the drug effects ($F=0.01, 0.3$) nor the drug $\times$ trials effects ($F=2.3, 1.9$) were significant in condition a or b ($P>0.1$) for all comparisons. Thus, cycloheximide exerted no effect during prolonged testing of mice which had already been trained.

trials the learning curves diverge, and thereafter the cycloheximide group did not improve as rapidly as the saline group (Fig. 1).

The divergence of the learning curves at trials fifteen to twenty-five occurred about 40 min after drug injection. At about 45 min after drug injection, mice also become markedly hypoactive and remain so for several hours^{5,6}. Because of the temporal coincidence of these effects of cycloheximide on training and on locomotor activity, we specifically investigated the possibility that retarded acquisition in cycloheximide-treated mice might be related to depressed motor activity. Mice were trained 10 min, rather than 30 min, after subcutaneous injection of cycloheximide or saline. Since training for sixty-nine trials takes approximately 25 min, hypoactivity does not develop in this condition until after training is completed. Thus, if locomotor depression is the cause of the acquisition deficit, the deficit should not appear. Alternatively, if the learning deficit in cycloheximide-treated mice is related to inhibition of cerebral protein synthesis, which is greater than 95% both at 10 min and 30 min after injection, the deficit in acquisition should be about the same in both conditions. Fig. 1 indicates that a deficit did appear when training began 10 min after injection and that the divergence in learning curves was first noticeable beyond trials fifteen to twenty-five, whether training began 10 or 30 min after injection.

We also trained mice 210 min after injection of cycloheximide or saline. Mice are hypoactive at this time^{5,6} and are visibly sick, although only 80% of cerebral protein synthesis is inhibited at this time in this strain of mice. If the deficit in acquisition is due to locomotor depression or to cerebral abnormalities resulting from a period of extensive inhibition of protein synthesis, an impairment in acquisition should also be demonstrable in mice trained at this time. Alternatively, if the deficit which we have observed is due specifically to more than 80% inhibition of cerebral protein synthesis during training, a deficit might not appear in mice trained 210 min after injection. No deficit was observed in this condition (Fig. 1).

We also considered the possibility that cycloheximide might interfere with performance by simply preventing mice from ever executing a high percentage of correct choices in this task. Saline-treated mice which had been trained for sixty-nine trials were divided into matched groups and 1 day later were retested by exposing them to sixty-nine additional trials 30 min or 210 min after cycloheximide or saline. If protein synthesis inhibition or side effects of the drug make it difficult to achieve high levels of performance in this discrimination task, then

performance should be impaired by cycloheximide injection before retest. Alternatively, if the deficit is related to inhibition of protein synthesis required specifically for the development of memory during initial learning, then performance of an already established habit should not be impaired by cycloheximide injection before retest. The results indicate that cycloheximide had no measurable effect on performance of the previously learned habit (Fig. 2). All groups maintained performance between 85–100% for the entire session.

These results indicate that within minutes after the beginning of training improvement in performance may be antagonized by cycloheximide. The results further indicate that hypoactivity produced by cycloheximide is not the cause of this effect and that cycloheximide does not prevent a high level of performance if prior training has occurred. We therefore suggest that a memory storage process dependent on protein synthesis may be required for as long as improvement in performance within minutes after the onset of training. In other experimental situations^{1,2,7-9}, this may have been overlooked, because only brief training was given. Reasons why normal retention is observed for 3 h after training^{1,2} in these situations have been considered previously³.

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***Dactylaria gallopava*, a Cause of Avian Encephalitis, in Hot Spring Effluents, Thermal Soils and Self-heated Coal Waste Piles**

THE hyphomycetous fungus *Dactylaria* (= *Diplorhynchium* = *Scolecobasidium*) *gallopava* (W. B. Cooke) Bhatt and Kendrick¹ was originally described as a causal agent of encephalitis in turkey poult². Because of new outbreaks of encephalitis in turkeys and chickens caused by *D. gallopava* (H. G. Blalock, W. T. Derieux, L. K. Georg and M. Ranck, personal communications), the widespread occurrence of *D. gallopava* in natural and man-made heated habitats should be noted.

We have isolated *D. gallopava* from geothermal habitats and from self-heated coal waste piles (Table 1). The 393 samples examined represented a wide range of pH values (<2 to >10). The fungus was isolated from thirty-one samples, all acidic (pH 2.1 to 5.9), suggesting that this is its preferential habitat in nature.

Samples were enriched at 37 and 47–50° C using several natural and artificial substrates. Sabouraud dextrose agar (Difco) plates (pH 5.6), with 100 µg ml⁻¹ of the thermostable antibiotic gentamicin sulphate, were best suited for detection and enumeration of *D. gallopava*; a distinctive reddish-purple pigment appeared in the agar beneath even young colonies.

Evidence for growth in natural habitats was obtained by observation of microscope slides which had been placed in hot spring effluents and thermal soils for differing periods of time, the habitats having a wide range of temperature (ambient to 87° C) and pH (1.7 to 8.4). At several hot, acid sites, a microbial mat composed of *Cyanidium caldarium* (a unicellular eukaryotic alga), *Dactylaria gallopava* and *Bacillus coagulans* formed on immersion slides; the structure of this mat was the same as on natural substrates. Structural and ecological relationships of the components of the mat will be reported elsewhere³. In aquatic habitats, impaction of the distinctive 1-septate, apiculate conidia of *D. gallopava* on the slides was followed by germination and development of radial microcolonies which could be traced to germinated conidia; a branched, septate mycelium subsequently developed. In soils, immersion slides bore conidiating colonies.

Further evidence for growth of *D. gallopava* in natural habitats is the occurrence in foam of its spores, germinated spores, hyphal networks traceable to spores and spores attached to conidiophores. This foam, which forms in turbulent regions on hot spring effluents, had the same pH value as the underlying waters and was only slightly cooler. One foam sample contained approximately 2×10^6 conidia ml⁻¹ of the liquid obtained from the foam. Germinated conidia also occurred in microbial mats in hot spring effluents.

Occurrence of *D. gallopava* in coal waste piles in England has been reported^{4,5}. We isolated the fungus from two of 250 samples from thirty-five self-heating coal waste piles in Pennsylvania and Indiana. Most of our samples were acid and were from sites having temperatures compatible with growth of *D. gallopava*.

Growth in pure culture occurred at both 20 and 50° C, although growth was slight at 50° C; rapid growth and conidiation occurred on Sabouraud dextrose agar at 37° C. To determine whether the apparent preference of the fungus for acid habitats was due to restrictive growth capacities at non-acid pH values, growth was measured in a malt extract medium adjusted to various pH values. Dry weight increase at pH 8.75 was excellent and was approximately the same as at pH 1.9 and at intermediate values; the fungus is therefore not obligately acidophilic. The fungus did not degrade filter paper at pH 3 or 7, nor did it clear Walseth acid-swollen cellulose⁶ at pH 6.

H. G. Blalock and W. T. Derieux have established pathogenicity of our isolate 141-2 from Yellowstone National Park

(personal communication). Day-old turkey poultts were inoculated intratracheally and the fungus was re-isolated from the brains of birds that died.

We conclude that *D. gallopava* occurs and grows in effluents of acid hot springs and in acid thermal soils; it also occurs in self-heated coal waste piles. Many species of thermophilic and thermotolerant fungi isolated from natural thermal habitats^{7,8} similarly occur in man-made heated habitats far from natural thermal sites^{4,9–11}. As temperatures in the range of mammalian and avian body temperatures exist in many geothermal sites, these habitats might be natural reservoirs for pathogenic microorganisms, and further search for pathogens in such locations is warranted.

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Table 1 Sample Sites which yielded *Dactylaria gallopava**

Sample site	Temperature†	pH‡
Thermal soil, Roaring Mountain, YNP§	42–43° C	4.5
Thermal soil, Solfatara Plateau, YNP	38.5–49.5	4.0
Thermal soil, Rush Lake Meadow, YNP	57.8–61.5	4.3
Thermal soil, Sylvan Springs, YNP	29	2.1
Hot spring effluent, Nymph Creek, YNP	50	2.8
Hot spring effluent, Sylvan Springs, YNP	48	2.9
Hot spring effluent, Ebro Springs, YNP	43	2.9
Hot spring effluent, Cyanidium Creek, YNP	46	3.0
Coal waste pile, Sonman, Pennsylvania	36–68	5.9
Coal waste pile, Mather, Pennsylvania	35–71	3.5

* Several sites yielded more than one positive sample.

† Using an electronic thermometer (Yellow Springs Instrument Co., Model 42 SC, with Model 408 "banjo" probe).

‡ By pH meters. Soil and coal waste samples were mixed with an equal volume of distilled water.

§ Yellowstone National Park. Rush Lake Meadow, Solfatara Plateau, Nymph Creek and Cyanidium Creek are unofficial names; exact locations and additional habitat data are available^{12–14}.

Thermal Regulation in Sail Lizards

THE extinct Order Pelycosauria contained several genera of reptiles characterized by extreme elongation of the neural spines of the vertebrae, which in life supported an area of membrane forming a "sail"^{1–3}. *Dimetrodon grandis* was the end form of an evolutionary series of pelycosaurs that had tended to develop increasingly large sails². Many suggestions have been made about the function of the sail, as camouflage among reeds while it waited for prey, for sexual display, or literally as a sail while swimming². Romer and Price² first suggested that it served a mechanical function and strengthened the backbone, but Romer³ later realized that the sail had evolved with features strongly suggesting an early attempt at temperature regulation. The spines are grooved anteriorly and posteriorly to house blood vessels carrying a rich supply of blood to the sail^{3–5}.

Dimetrodon grandis is found in the Autunian formation of the Permian of Texas. The environment was semi-arid with a xerophytic flora; yet enough water was present in certain areas to support a varied population of amphibians². *Dimetrodon*

was the dominant carnivore, and possible prey included the herbivorous pelycosaurs *Edaphosaurus* and *Cotylorhynchus* and the amphibian *Eryops*². Presumably, the environment was warm and sunny enough for the pelycosaurs to bask in the Sun in the normal reptilian manner⁶, and it is possible that, as in arid areas today, there was considerable diurnal variation in temperature⁷.

Assuming the present solar constant of 20,000 calories $\text{min}^{-1} \text{m}^{-2}$, the maximum rate of heating *Dimetrodon* would be $20 A/W \text{ K min}^{-1}$, where A is the projected area (m^2) and W is the weight (kg). Allowing for incomplete absorption, atmospheric attenuation and possible brightening of the Sun in the last 260 million years, a rate of heating of $10 A/W \text{ K min}^{-1}$ was unlikely to have been exceeded under natural conditions. This is approximately the rate of heating in American alligators when exposed to the Sun⁸. The weight of *Dimetrodon grandis* was estimated by Romer and Price² as 250 kg. We have found that the lateral projected area is 1.88 m^2 , the sail accounting for 1.15 m^2 of this. Taking 26°C as the voluntary minimum temperature and 32°C as the activity temperature⁸, and assuming that *Dimetrodon* basked laterally to the Sun's rays in a similar manner to other reptiles^{6,9}, the value of the sail as a device to hasten heating can be quantified by using the formula above. The body temperature would have been raised from 26°C to 32°C in 205 min without the sail, but would have taken only 80 min with it.

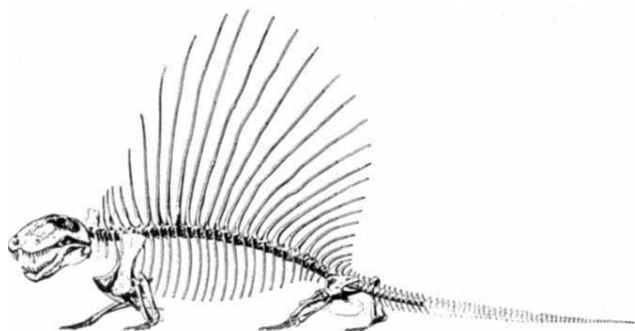


Fig. 1 Skeletal restoration of *Dimetrodon grandis* (from ref. 2).

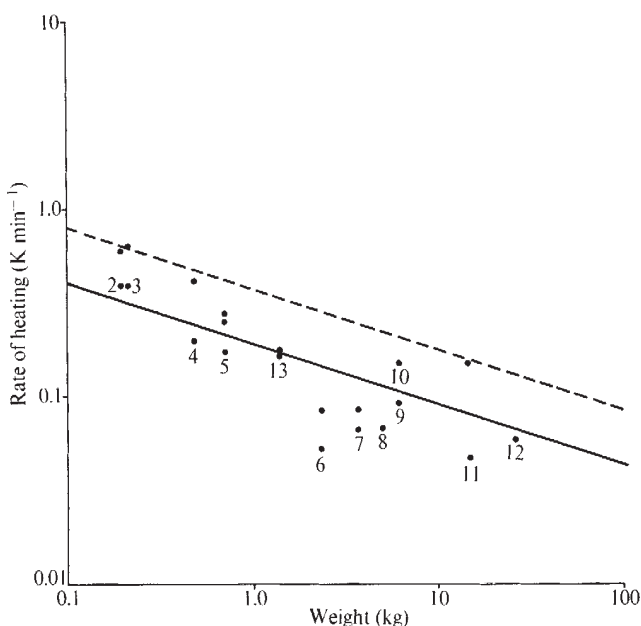


Fig. 2 Rate of heating of American alligators of different weights exposed to sunlight. Data from Colbert *et al.*⁸. Slope (—) is $-1/3$ (about $10 A/W$).

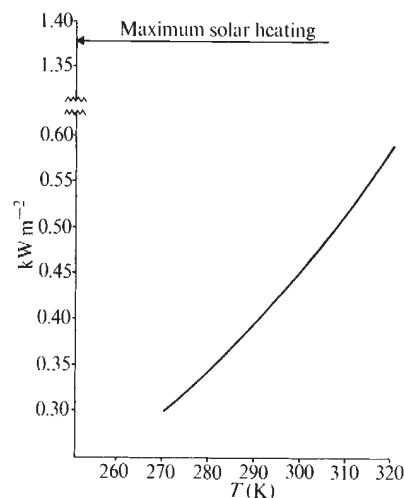


Fig. 3 Heat radiation from the sail of *Dimetrodon*.

The sail was also capable of radiating heat from the animal. To do this *Dimetrodon* would have assumed a position in which it presented a minimum area to the Sun, that is facing anteriorly towards it, allowing the sail to radiate to the sky from both its surfaces. The projected area exposed to insolation in this position is only 0.21 m^2 . Living reptiles orientate in this manner⁹ when their temperature rises above the normal activity range and approaches the critical maximum of 38°C to 43°C , according to the species.

The maximum radiation possible is shown in Fig. 3; at a realistic body temperature of 40°C it is 0.54 kW m^{-2} . Allowing for imperfect emissivity and radiation back from the environment, the net value is unlikely to have exceeded half this, but even so this still amounts to 0.6 kW being lost from the 2.3 m^2 area of the sail.

These figures lend quantitative support to the hypothesis³ that the sail conferred advantage through thermal regulation. Faster attainment of the activity temperature in the morning was an obvious advantage to a carnivorous reptile feeding on other large poikilothermic animals. *Dimetrodon grandis* would have been able to reach an active state and attack prey while they were still torpid or sluggish. During the hot part of the day the sail would have acted to radiate away excess heat; this effect could be an important adaptation in a reptile which was too large to seek shade behind small stones or in rock crevices⁹ in the manner of small living reptiles. In the evening *Dimetrodon* could have gained extra activity time, in comparison with a sail-less pelycosaur of the same A/W ratio, by restricting blood flow to the sail. The sail could therefore prolong the total time in which *Dimetrodon* could be active in any 24 h.

Our conclusions are reinforced if, as seems probable, the controlling adaptations had become highly refined. In addition to adjustments of blood supply, the degree of blackening may have been under nervous or hormonal control. Some lizards⁹ which are black when basking to catch the maximum radiant energy can change to white when oriented head-on to the Sun and emitting heat. It is possible that *Dimetrodon* (or indeed living reptiles) may be black in the infrared to radiate heat more effectively, while appearing white in visible light. Visible and infrared emissivities of *Dimetrodon* may have been separately adjustable according to the thermal state of the animals.

We thank Professor Romer for permission to use Fig. 1

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External Ocelli in Lepidoptera Previously Considered to be Anocellate

DORSAL ocelli are simple photoreceptors found in nymphal and adult hemimetabolous insects and adult holometabolous insects^{1,2}. They were thought to have a variable distribution, and to be absent in many representatives of several insect orders; in Lepidoptera several families have been considered to be entirely or partially anocellate³⁻⁴. In sphingids it has been reported that their large superposition eyes have assumed the function of the ocelli⁴, but it is now known that the sphingids are not anocellate. Ocelli were described within the

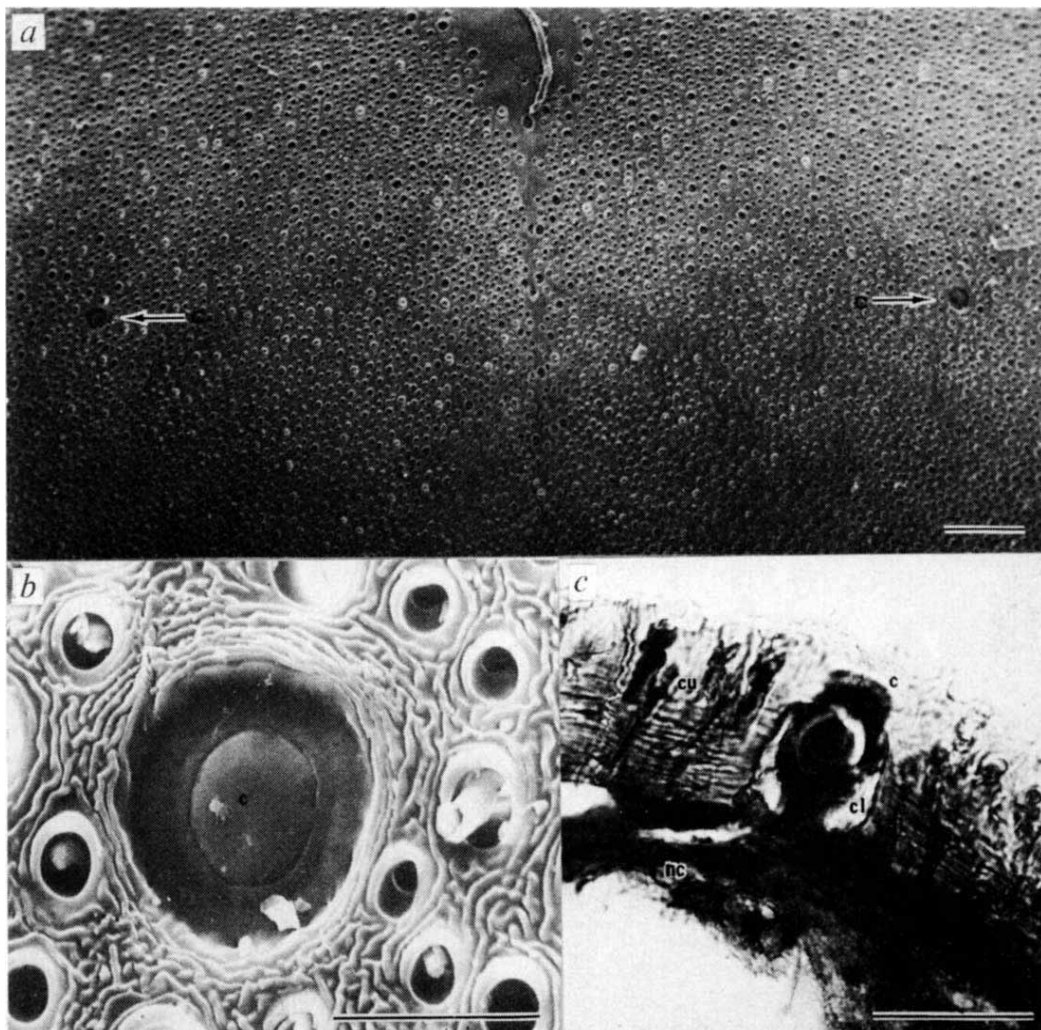
dorsal protocerebrum in the adult of *Sphinx convulvi* by Berlese⁵ and recently internal ocelli have been reported in several adult sphingids, saturniids and citheroniids⁶. There have been no descriptions of external ocelli in sphingids, saturniids, citheroniids, or any Ropalocera⁷.

We re-examined the structure of ocelli in moths previously described as being anocellate. Removal of scales on the vertex of the head posterior to the antennae and dorso-medial to the compound eyes revealed a small pair of external corneal lenses (Fig. 1a and b). These convex structures were located at the bottom of a round cuticular depression about 26 μ m diameter. Similar, slightly smaller structures were found in the several species of butterflies examined (Table 1).

Longitudinal sections through this external cornea revealed several underlying cells believed to be reticular cells (Fig. 1c). In the sphingid specimens observed, a nerve branch arising from the bulb of the internal ocellus could be traced to the external structure (Fig. 2). Although similar nerves were not observed in all specimens examined, the possibility of their existence cannot be ruled out at this time. Similarly, internal ocelli have not been detected in all Ropalocera; they are, however, present in Hesperidae and a structure believed to be an internal ocellus has been observed lying on the dorsal side of the protocerebrum in the pierid, *Colias philodice* (Fig. 3). We believe similar structures will be found in other butterflies as well.

This is the first report of external ocelli in Lepidoptera previously described as being anocellate. Eaton⁸ reported that removal of the scales on the vertex of certain sphingids,

Fig. 1 a, Scanning electron micrograph of *Manduca sexta* (Lepidoptera: Sphingidae) head showing the two corneal lenses. The posterior of the head capsule is up. Bar equals 100 μ . b, Higher magnification of the cornea on the left side of a. c, Light micrograph of a longitudinal section through the external ocellus of *Calasymbolous ex-caecata* (Lepidoptera: Sphingidae) showing cornea and a nerve extending from the cells beneath the cornea. Bar in b and c equals 20 μ m. c, Cornea; cl, probable retinula cells beneath cornea; cu, cuticle; nc, nerve leading to cells beneath cornea.



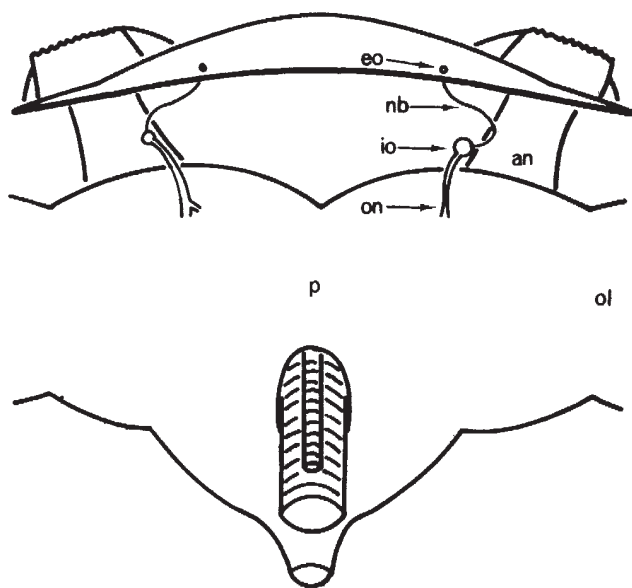


Fig. 2 Posterior view of the brain of *M. sexta* showing the internal ocellus and the nerve branch to the external ocellus. The asymmetry between the two ocelli is an example of the variation in structure frequently observed. an, Antennal nerve; eo, external ocellus; io, internal ocellus; nb, nerve branch; on, ocellar nerve; ol, optic lobe; p, protocerebrum.

Table 1 Lepidoptera reported to be Anocellate having External Ocelli

Heterocera	
Sphingidae: <i>Calasymbolous amyntor</i> <i>C. excaecata</i> <i>C. myops</i> <i>Darapsa myron</i> <i>D. pholus</i> <i>D. versicolor</i> <i>Herse cingulata</i> <i>Hyoicus chersis</i> <i>H. drupiferanum</i> <i>Lapara coniferarum</i> <i>Manduca quinque maculata</i> <i>M. rustica</i> <i>M. sexta</i> <i>Pholus achemon</i> <i>P. pandorus</i> <i>Spectrum lineata</i> <i>Sphinx jamaicensis</i>	Saturniidae: <i>Actias luna</i> <i>Automeris io</i> <i>Telea polyphemus</i> Citheroniidae: <i>Anisota rubicunda</i> <i>Citheronia regalis</i> <i>C. sepulchralis</i> <i>Eacles imperialis</i> Arctiidae: <i>Lithosiinae</i> <i>Hypoprepia miniata</i>
Ropalocera	
Papilionidae: <i>Papilio polyxenes</i> <i>P. troilus</i> Pieridae: <i>Colias eurytheme</i> <i>C. interior</i> <i>C. philodice</i> <i>Pieris rapae</i> Danaidae: <i>Danaus plexippus</i> Satyridae: <i>Cercyonis pegala</i>	Nymphalidae: <i>Euphydryas phaeton</i> <i>Limnitis archippus</i> <i>Polygonia comma</i> <i>Speyeria aphrodite</i> <i>S. cybele</i> <i>S. diana</i> <i>S. idalia</i> <i>Vanessa atlanta</i> Libytheidae: <i>Libytheana bachmanii</i> Lycanidae: <i>Celastrina argiolus pseudargiolus</i> Hesperiidae: <i>Epargyreus clarus</i> <i>Thorybes pylades</i>

saturniids and citheroniids revealed an evenly pigmented cuticle with no lens-like structures present. This earlier oversight was due to the small size and the coloration of the corneal lenses along with the fact that they are not located in the usual position of the lepidopteran ocellar cornea. In our study all "anocellate" Lepidoptera examined possessed small external ocelli.

The presence of a nerve branch from the internal to the external ocellus in some moths indicates either; the presence of synapses of sense cells of the external ocellus with second order neurones whose somata lie in the brain, or extension of sense cell fibres whose somata lie in the internal ocellus (which is unlikely) or the presence of internuncial neurones between sense cell fibres from the external ocellus and fibres from somata within the brain (which is improbable). We considered the possibility that the nerve branch might act as a light-guide to conduct light to the internal ocellus but we rejected it owing to the tortuous route taken by this nerve.

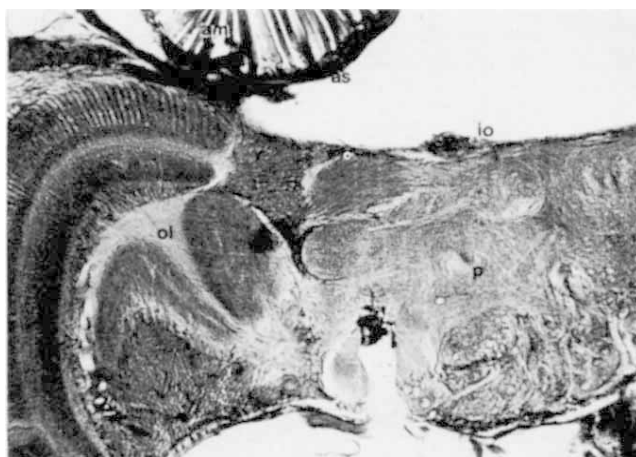


Fig. 3 Light micrograph of a frontal section through the head of a clouded sulphur butterfly *Colias philodice* (Lepidoptera: Pieridae) showing the left side of the protocerebrum, optic lobe and possible internal ocellus. am, Antennal muscles; as, antennal sclerite; io, internal ocellus; ol, optic lobe; p, protocerebrum.

Perhaps the most significant aspect of our study is the presence of an external ocellus in "anocellate" Lepidoptera which in certain moths is also connected to the internal ocellus by a nerve branch. The possibility of a two-part ocellus in these moths therefore exists.

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BOOK REVIEWS

Mathematical Metaphor in Development

Stabilité Structurale et Morphogénèse: Essai d'une Théorie Générale des Modèles. By René Thom. Edited by A. S. Wightman. Preface by C. H. Waddington. Pp. 362. (W. A. Benjamin: New York; Addison-Wesley: Massachusetts, November 1972.) \$28.

THIS book by one of the world's foremost geometers is remarkable in many ways, but perhaps most notably for the breadth of the enquiry undertaken and for the unity and coherence of vision which are achieved. What we are offered is a new mathematical metaphor, created by Thom in response to the challenge of rendering intelligible the world of structure and form. The primary inspiration for this came from reading the works of biologists such as D'Arcy Thompson and C. H. Waddington on the origin and nature of organic form as revealed in plant and animal morphogenesis. The strong geometrical imagery of these writings provided the germ for a mathematical theorem which is the foundation of a complex edifice of analytical constructs applied sometimes with insight, sometimes without, to a wide range of biological problems.

Despite certain shortcomings, the book gave me a sense of liberation and enlightenment akin to what I imagine Ptolemaic astronomers may have felt when offered Copernican heliocentric geometry as an alternative to the endless epicyclic calculations required by the geocentric picture. The Ptolemaic system that I feel burdened by is biological model-building which proceeds from the kinetics of molecular and cellular interactions through non-linear differential equations to the study of their solutions in the neighbourhood of singularities. Created by Newton and Leibnitz in response to the necessity for a quantitative rendering of the Copernican model, the differential calculus was not intended to deal with discontinuity and structure but with continuous, smooth planetary motions. Poincaré initiated a more general approach to the study of discontinuities or bifurcations of dynamical sys-

tems about 100 years ago, and it is the recent flowering of this method in the hands of Russian, French, and American mathematicians which provides the context for Thom's work. This shifts the focus from continuity to discontinuity, facing directly the problem of describing mathematically how singularities arise in natural processes and generate discrete shapes and forms (including symbols). Since these processes vary with the initial state, it is necessary to forge an analytical tool which allows one to explore the possible structures which can arise in a given dynamical context and the stability of their structural emergences or unfoldings (hence a systematics for their classification). This is what Thom achieves in his basic theorem, presented in some detail in chapter 3. I cannot pretend to have followed all the details of this theorem, but, as it is the basis of the whole book, a few words of description are appropriate.

It is acknowledged by the topological *cognoscenti* that very little is known about the general properties of dynamical systems as described by the flows or trajectories on a manifold. Faced with an amorphous state of general theory, a mathematician must be guided by his insight and intuition in seeking constraints which generate new mathematical structures in terms of which the "real" world can be represented. Thom uses two fundamental postulates: (1) a general one of structural stability which embodies a basic principle about legitimate, intelligible models of natural process (hence the sub-title of the book); and (2) a specific hypothesis which requires that the dynamical systems studied be describable by gradient fields of potential functions. The mathematical entities which emerge from these constraints are the seven (and only seven) elementary ways in which the particular class of dynamical process considered by the theorem can give rise to discontinuities or singularities (called catastrophes) in ordinary space-time, generating recognizable structures or forms in a stable

and repeatable manner. These discontinuities act as local organizing centres of the dynamical process, a space-time structure emerging in a defined manner as described by the universal unfolding of the singularity (or its enfolding, if the process is reversed). If the dynamical space is insufficiently polarized for there to be a local coordinate system, then another much more complex set of singularities can occur, called generalized catastrophes. Their properties have not yet been analysed in any detail.

The postulates of the theorem have been criticized on the grounds that they are both too general (for example, they are relative to an unspecified diffeomorphism on the space one uses to describe a process of interest, such as a biochemical concentration space), and too specific (for example, gradient field systems are a very restricted set of those that are possible). I think these criticisms tend to cancel one another out. The main point is that these postulates result in a geometrical model which is radically (that is, at the root) non-linear and lends itself naturally to description in the same language as that used in morphogenesis: organizing centres, polarity, morphogenetic fields, the development or unfolding of a centre, interactions between competing organizers or attractors and so on. Thom's own position is essentially Aristotelian (he would prefer Heraclitian or Cartesian): the primary qualities demanded of a model or a metaphor besides precision and rigour are intelligibility and appropriateness for the description of natural, and particularly biological, process. Quantitative power, computability, is secondary to understanding and meaning. Every concept Thom uses to supplement the basic theory of catastrophes in order to give it the dynamic plasticity and complexity required for biological explanation, such as the concepts of thermodynamic coupling, resonance, phase transition, and so on, is used in a purely descriptive spirit and will no doubt irritate those looking for an exact quantitative

test of the model. Such a test is not available for the principal reason that as yet no calculus exists which allows one to use Thom's theory of the unfoldings or enfoldings of organizing centres of catastrophes in a computational rather than a geometrical manner. Thus any test of the theory at this stage in its development must be qualitative, in terms of intelligibility and appropriateness, and this is difficult for minds more receptive to local goodness of fit than to global meaning. But let me try.

I think it would be fair to say that practically every specific biological process which is described and analysed by the theory advanced in this book is more thoroughly and adequately accounted for at the moment by a model constructed in terms of the concepts germane to the level of the problem, whether molecular, cellular, physiological, genetic, or psychological. There are many points where I find the application of the theory excessively literal, rather like regarding the burning of a candle and the respiration of glucose as identical; which is not to deny a fundamental similarity. For example, in the treatment of the nucleus as a chemostat (page 279) the interaction of chromosome and cytoplasm is interpreted as a hydrodynamic singularity, a diffusional shock wave across the membrane which persists until nucleo-cytoplasmic control equilibrium is attained. I find it difficult to imagine such a shock wave lasting for periods of hours, the relaxation time of such responses, given the rapidity of diffusional equilibration. Again, the attempt to provide a Lamarckian interpretation for the evolutionary origins of organs, proteins, and genes and the appeal to plasmagenesis is basically unconvincing. There are undoubtedly ways in which heritable metastable states of chromosomes, membranes and organelles can be induced by physiological stress ("shock waves"), but these must be thought out much more subtly in relation to current knowledge than we are given here. Chapters 9-12 in fact are written in the style of an extended, free metaphor and a great deal of their content cannot, I find, be taken literally. On the other hand they are full of improvisation and rich in suggestion. For example, the analysis of the relationships between gastrulation in amphibians, reptiles, and birds (pages 180-184) is very ingenious despite inaccuracies of fact here and elsewhere (closure of the blastopore in amphibia takes hours, not seconds; mesoderm induces ectoderm not *vice versa*), and suggests some interesting comparative embryological experiments, at least between the cold-blooded genera.

This leads us to ask the question

whether Thom's theory tells us anything we did not already know in more detail. I think it does, in two important respects. First, although it does not explain the intricate architecture that evolution has built into biological structure-generating processes, the mathematical theory is capable of such elaboration in relation to the details of the universal unfolding of a singularity or organizing centre. In this sense it suggests a direction for the development of a calculus that copes easily with non-linearity and discontinuity, with stability and structure. And second, the theory directs our attention to the very difficult problem of origins: what is the natural basis for the emergence of the extraordinary complexity of biological process? Thom believes with Heraclitus that nature is one: that the structures we see in the physical world such as the breaking wave or the whirlpool are generated by dynamical germs or centres that are geometrically similar to those operating in organogenesis or enzyme action, for example. The difference is in the detail of the unfolding of the singularity, the biological system exercising precise control via proteins, membranes, electrical or material gradients, and so on. This vision of continuity is most powerful in the relation which Thom describes between morphogenetic and behavioural fields in chapter 13, providing what I found to be an inspired though exceedingly sketchy conceptual framework for understanding how mind and symbol emerge from the biological substratum, the essential problem of structuralism. I suspect that it may be here that the theory could come most importantly to our aid, providing a bridge of intelligibility across a gap which at present seems so wide.

This book is to be regarded as outlining a method of inquiry, as Thom himself has emphasized; and this method may or may not succeed. In biology we will discover this only by working with the model, developing the requisite calculus and attempting to fit it to the biological data. An impressive example of this procedure is provided by E. C. Zeeman, a lucid exponent of Thomism, in his article in the book *Towards a Theoretical Biology* (edit. by C. H. Waddington), 4, 8; Edinburgh University Press, 1972). In the same volume there is an article by Thom on "Structuralism and Biology" (pages 68-82), while his article in volume 3 of this series (pages 89-116) gives the essence of the method in English. Even if this model fails, the sustained inspiration and the vast scope of the book put it firmly into the best tradition of natural philosophy, the search for a rigorous and meaningful synthesis of the fragmented strands of contemporary knowledge.

B. C. GOODWIN

Infrared in Space

Infrared Detection Techniques for Space Research. Edited by V. Manno and J. Ring. (Proceedings of the 5th ESLAB/ESRIN Symposium, held in Noordwijk, The Netherlands, June 1971.) Pp. xi+344. (D. Reidel: Dordrecht, 1972.) Dfl. 90.

THE bulk of this book contains information and data on a variety of techniques and facilities used in balloon, aircraft, rocket and satellite borne infrared observations, and is divided into six fairly well defined sections. Giving some perspective to the technicalities that follow, it begins with a short review of results obtained in infrared astronomy up to the middle of 1971. A section follows on the currently used telescopes and related systems for upper atmospheric and space vehicles. Two balloon borne systems in operational use, of 30 cm and 39 cm aperture with magnetometer and star tracking guidance respectively, and systems of 32 cm and 90 cm for aircraft use are described. There are contributions on interferometry and radiometry from rockets and satellites and observational data on the spectral sky radiance as a function of altitude are provided. Also included in the section is a description of a helium cooled interferometer to measure the far infrared cosmic background radiation from balloon altitudes.

The third section deals with detectors, starting with a statement of fundamentals and the present state of the art and continuing with description and comparative performances of some cooled colometers and a contribution on the Josephson effect.

Fundamentals of space borne cooling systems are next reviewed and likely lines of development are indicated. One of the outstanding needs before astronomy in the middle and far infrared becomes possible from Earth satellites is the development of suitable long-term cryogenic systems for liquid helium temperatures. Although it seems a pity that this work contains only one contribution on the subject, it may perhaps be optimistically assumed that adequate solutions are nearer than the published literature would suggest. For all other than satellite systems the major problems seem to have been overcome, as indicated by the operational success of a number of helium cooled detection systems. A wealth of information follows on the design and fabrication of filters for far infrared work. Much of this section is devoted to the use of metal mesh filters and performance data are given on a number of practical designs.

A fairly full section is given on the use and principles of interferometer techniques and the book closes

with a short section of discussions. The book contains a large amount of relevant information on the subject matter for those active in the field. As well as this, the layout and presentation are such that there is much to interest the non-specialist.

D. K. AITKEN

Ganglion Growth Factors

Nerve Growth Factor and Its Antiserum. Edited by E. Zaimis and J. Knight. (Papers presented at a Symposium held at University College, London, April 1971.) Pp. xi+273. (Athlone: London, June 1972. Distributed by Tiptree Book Services Ltd.)

THIS volume consists of a collection of two dozen papers presented at a symposium held not quite two years ago at University College, London. Its content reflects the excitement, uncertainties, and controversies of a newly and rapidly developing field and points the direction of future research.

Nearly twenty years ago Dr Rita Levi-Montalcini and her associates discovered protein factors which stimulate growth of ganglionic neurones both *in vivo* and *in vitro*. The startling effects of antibodies to these proteins on the development of the sympathetic nervous system indicate their physiological importance. During the last ten years other investigators have been stimulated to examine the nature and origin of the protein factors and the biochemical and physiological consequences of administration of the antibodies to these factors.

In the introduction, the editors have succinctly outlined the purposes and objectives of the symposium. The first section is devoted to work which has been done to define the nature and actions of the nerve growth factor, while a second section considers antibodies to NGF, and a brief third section deals with the problems in the assay of NGF and its antibody.

The opening chapters present in adequate detail the methods for purification and characterization of NGF from snake venoms and mouse submaxillary glands. These factors appear clearly different from each other. The well known biological effects of NGF are reviewed by its discoverer and her collaborators along with a report of more recent observations on the subcellular distribution of NGF. The effects of NGF on growth of sympathetic tissues are well illustrated in the paper by Professor Zaimis, after which the biochemical and fine structural changes induced in sympathetic ganglia *in vivo* and *in vitro* are reviewed.

The second section of the volume is concerned with the effects of inhibition

by antibodies to NGF of development of the sympathetic nervous system. The consequences of immunosympathectomy on the tissue content and metabolism of amines, and cardiovascular responses and behavioural patterns (by motor activity on exposure to cold) and use of immunosympathectomy as a pharmacological tool, are considered. In the last brief section on assay of NGF and its antibodies, some pitfalls in assays are pointed out and the potential for development of new sensitive radioimmunoassays for NGF is indicated.

The various papers are not of uniform detail or quality, but this may reflect the uneven advance of a new field. The editors have not imposed stylistic restrictions on the authors. One feels that a report of discussions of the papers might have enhanced the value of the volume since discrepancies and differences of opinion (for example, the similarities and dissimilarities of NGF from different sources), although recognized, pass without comment.

This is a cohesive, well balanced volume which may be considered a milestone marking a point in the development of a new and exciting field. There are wide implications to embryology and plasticity of the nervous system. It should be read by those interested in the problems related to the development of the nervous system as well as investigators concerned with mechanisms of the sympathetic nervous system.

I. J. KOPIN

Pollution by Combustion

Emissions from Continuous Combustion Systems. Edited by W. Cornelius and William G. Agnew. (Proceedings of a Symposium held at the General Motors Research Laboratories, Warren, Michigan, September 1971.) Pp. x+479. (Plenum: New York and London, 1972.) \$29.

It is none too common to be able to read the papers from a serious symposium within a couple of years and so the publishers of these are to be congratulated. The excellent presentation, diagrams, graphs and photographs do much to add to the general worth of this collection of opinions from acknowledged international pundits in the field of combustion. Would-be readers must realize, however, that these papers—and their related edited discussions—require considerable knowledge of thermodynamics, in certain cases fairly advanced mathematics, and some acquaintance with gas turbine and furnace technicalities. Although the ultimate purpose of the symposium was a general review of pollution from these sources and what can be done to reduce it, the speakers dealt with

how to do it in the intimate terms of their trades.

General Motors Research Laboratories has held fifteen annual symposia to review the "state of the art" of the various sciences and techniques related to heat engines. The meetings last two days and about sixty delegates are invited after careful selection with a view to bringing together the élite of the academic, industrial and governmental brains concerned with the theme of the year. The choice of the environmental effect of emissions from the combustion of fossil fuels was becoming topical in 1971 and is of paramount importance today.

The symposium was given in four sessions: "Modelling continuous combustion", chaired by J. P. Longwell of Esso Research and Engineering Company; "Pollutant formation and destruction processes", chaired by G. C. Williams of MIT; "Effects of operating conditions and fuel factors", chaired by A. H. Lefebvre of the Cranfield Institute of Technology; and "Power-plant emissions", chaired by P. S. Myers, University of Wisconsin. It would be invidious to name only some of the authors of the twenty-one papers, but the outstandingly clear, concise and objective symposium summary by W. G. Agnew gives a very clear picture of what was said; he also made a profound comment on the general understanding of the subject as appreciated internationally by the participants.

The first session showed the way in which flow through combustors can be partially simulated observationally with kinetic models and by mathematical analysis. The general impression one gets is that there is still a long way to go before models can be really useful. The second session was largely reports of research in progress on relating physical and chemical parameters for the further elimination of unburnt hydrocarbon waste and ways of tackling NO (nitrous oxide) formations. At present water injection seems the best, but rather troublesome, method of suppressing these corrosive products by keeping the temperature below their formation level. However, from the third session, it appeared that such cooler gases can mean less than stoichiometric combustion—and, inevitably, unburnt hydrocarbon contaminants. The papers suggested, in fact, a temperature "slot" for combustion between 1,500–1,800 K in order to give the "purest" efflux. Control of visible smoke, the hydrocarbon and CO residue, is now being put into practice, beginning before ignition with vaporizing fuel injectors like those fitted in the latest Olympus in Concorde 02, which flew in January of this year.

In the fourth session, a paper on how

emissions from stationary boiler powerplants are being controlled was an interesting insight into other people's problems. The remaining papers in this section covered gas turbine, steam and Stirling-cycle powerplants for vehicles, with a fascinating one about the work of the General Electric Company (US) on the control and reduction of emissions from aero gas turbines. From this company's experience it would appear that the engine makers are on the last lap—reducing that reek of unburnt kerosene from idling engines which assails the passenger at every modern airport.

A very useful reference for any company technical library, or for a college—bearing in mind that much of the material will be out of date in five years—but a trifle expensive for the individual's purse. JAMES HAY STEVENS

Madness and the Community

A History of the Mental Health Services. By Kathleen Jones. Pp. xiii + 414. (Routledge and Kegan Paul: London and Boston, December 1972.) £5.

"HISTORY," said Henry Ford, "is bunk." In spite of Professor Kathleen Jones's modest supporting conclusion that the only lesson to be learned from the past is the unpredictability of change, her splendid book drives the reader relentlessly to a number of invaluable general deductions. Perhaps the most important of these is that progress, seen in historical time, is advancing in spiral fashion, with the real forward movement along the axis being agonizingly slow compared with the apparent speed of advancement round the circle. A corollary of this is that the defects of one system of care are only too easily thought to be remediable by replacing it with a "new" system, which history reveals has already been tried and found to have its own defects.

This important book succinctly traces the evolution of attitudes to the mentally ill and the mentally handicapped through the documentary evidence available to the historian. What might otherwise be a dull catalogue of reformist speeches, parliamentary debating points, and successive legal enactments is brought to life by illuminating personal anecdotes. I am still haunted by the description of William Norris, who was confined continuously for nine years at Bethlem in a special iron apparatus which effectively prevented all but the smallest movements. On discovery in 1813, he was found to be quiet and rational, able to hold an intelligent conversation, and to read with comprehension. In

case the reader is inclined to dismiss such extremities of treatment as belonging to the past, I would remind him that even today nursing shortages often compel staff to put violent patients in solitary confinement in small cells, when technical treatments well known to be effective in modifying such disturbed behaviour could be used if sufficient skilled staff were available.

No literate person should neglect a close examination of Professor Jones's book, for its lessons are of general importance. Perhaps all schools should make it their major study of social history. Imaginatively treated, its subject matter could make a strong impact on a new generation who might then make the sustained effort necessary to resolve the underlying problem: constructing a society with a different value system, in which the understanding of people's needs makes neglect of any section unlikely. We must remember that the weak and the poor are under-privileged because we are over-privileged. We have devised a set of rules for an economic competition which ensures that we inevitably win and they inevitably lose.

Community care is the currently favoured panacea for the evils of asylums built by a previous generation to rescue pauper lunatics from community neglect. The cynic will conclude, after reading this history, that it is possible to neglect the mentally disordered in two ways: we can shut them up in remote, impoverished institutions, or we can push them out into the uncaring anonymity of the urban environment. Either way we can assume it is for their good, especially if the service doesn't cost the rest of us too much and we don't actually have to be involved. And when some enterprising journalist uncovers a few scandalous cases, we can always comfortably indulge in moral indignation, especially if someone else can be conveniently scapegoated.

Community care, then, history tells us, is not worse, nor necessarily better, than institutional care. Care is the operative word. At a time when pride is being taken at the fall in the number of psychiatric beds, the number of people in prison and the number of urban homeless are rising. We can only be certain that the quality of life of the mentally disordered is improving, and goes on improving, relative to the rest of us, if we base our monitoring system on a complete case register which enables us to follow people's progress and to supply their needs through a flexible system of treatment and care facilities of a high standard. The public must not be allowed the comfort of ignorance, nor short-lived concern after scandalous revelations. They must be constantly reminded of the needs of local people and the cost of

the provision of satisfactory services.

The problem can then be seen in its proper historical perspective—the mentally ill and the mentally handicapped are neglected by us. Unless we vote with our money, and personally befriend the disordered and the deviant, the next two hundred and fifty years will be much like the last.

The question this book poses is, do we care? JACK BAVIN

Distributions

Distributions in Statistics: Continuous Multivariate Distributions. By Norman L. Johnson and Samuel Kotz. Pp. 331. (John Wiley: New York and London, November 1972.) £7.50.

THIS is the fourth of a series in which the authors systematically review what is known about statistical distributions. The three earlier books dealt with discrete distributions and continuous univariate distributions (two volumes). This present volume, undoubtedly the toughest, completes the set; multivariate discontinuous distributions were covered in the first volume.

There is a sharp contrast between the wealth of mathematical forms with which we can express the frequency or probability distributions of univariate theory and the relatively few tractable forms available in multivariate theory. The number of parameters concerned increases alarmingly with the dimension of the distribution—even for the simplest case, the multivariate Gaussian (normal) form, the parameters increase as the square of the dimension number. The evaluation of numerical probabilities by integration is a formidable task even for two dimensions and even with the aid of the electronic computer. Some entirely new types of problem arise which are not encountered in univariate theory; for example, finding the distribution of the eigenvalues of a covariance matrix, which are not, unlike most statistics, algebraic functions of the observations. Altogether, the theory of multivariate distributions poses the most difficult problems in mathematical statistics.

One therefore gives an unqualified welcome to this book, which systematically reviews the present state of knowledge and pulls together a somewhat scattered literature in a consecutive development. As a textbook it would be heavy going except for the specialist. As a work of reference it is invaluable—over 700 titles are given. A comprehensive coverage of such a kind is to some extent a labour of love and statisticians everywhere should be grateful to the authors for the amount of effort which has gone to the completion of this work. M. G. KENDALL

Biological Compartments

Compartmental Analysis in Biology and Medicine: Kinetics of Distribution of Tracer-labelled Materials. By J. A. Jacquez. Pp. xiv+237. (Elsevier: Amsterdam, London and New York, 1972.) Dfl. 77.50; \$24.25.

COMPARTMENTS in a system interact with one another and perhaps with the surrounding environment. A compartment is an amount of material acting kinetically like a distinct well-mixed amount of the material. Separation between compartments does occur in various biological systems, for chemical as well as physical reasons. Compartments can be such things as plasma, interstitial and intracellular spaces. Hence the mathematical study of compartmental system models is useful, that of linear systems having counterparts in other areas of applied mathematics.

Inevitably the practical interpretation of compartmental analysis raises difficulties and arguments, and systems of order higher than linear are not easy to analyse. Nevertheless this book is an interesting survey of the present state of the art.

Necessary basic mathematics, covered in early chapters, comprises linear differential equations, vectors and matrices, and Laplace transforms: considerable facility in applying all these is needed to understand the book. This will indicate the appropriate level of readership.

It is in chapter 5 that biological interest really becomes aroused, by a study of radioactive tracer movement in steady state systems under suitable (and not unreasonable) assumptions. Henceforward, numerous references are made to the massive list of 455 papers (including some books) which appears at the end of the volume. This list is an excellent feature, but its presence only serves to make one wonder why space could not be found for answers to, or brief discussion of, the exercises at the ends of chapters.

Chapter 6 is concerned with systems partly compartmental and partly flowing, for example in some respiratory studies. Analysis in terms of experimentally observable functions can only be approximate, but does take the form of a compartmental system. Chapter 7 considers how one might set up a compartmental model from experimental data—very salutary after the almost entirely mathematical nature of the early part of the book—and chapter 8 introduces biological problems of varying complexity, and their solution by these methods.

After these two more practically biased chapters, the author moves from linear systems to introduce cases where experiments are long-term and so must allow for such things as daily (24-h) periods in bodily functions. Unfortunately too,

biological systems have a habit of containing random components: thus drug therapy has randomness in times of application, and even in amounts. Finally, the author picks a few points out of control theory, and in an interesting chapter 14 discusses some examples of compartmental control systems.

G. M. CLARKE

Microcapsules not Cells

Artificial Cells. By Thomas Ming Swi Chang. Pp. xiv+207. (Charles C. Thomas: Springfield, Illinois, June 1972.) \$16.

THE eye-catching title of this book immediately evokes curiosity and is likely to lead one to suppose that what may be predicted as achievable well beyond AD 2000 has already been accomplished in some quiet corner unbeknown to everybody. This is to some extent promulgated by the editor's preface connecting the studies with the synthesis of cells. Reference is made to forms of life on other planets and that the basic unit of such life could be different from the cell we know. All this seems to herald the shape of things to come in the book.

Authors are aware that the inclusion of a fashionable word in the title of a paper will send up the requests for reprints. A fashionable word is "cell" and in biology it stands for an extraordinary piece of machinery organized at the molecular level at a complexity that is almost beyond our belief and understanding. In the author's preface of the book we read: "Back in 1956 I was surprised to find that despite the fundamental importance of cells serious attempts had not been made to use available knowledge to investigate the feasibility of preparing artificial cells". We read on to find that "equipped with a borrowed clinical centrifuge, a few chemicals, a few glasswares and a few frustrating months" the author came up with samples of artificial cells. Each consisted of haemoglobin and enzymes from red cells enveloped in an ultra-thin spherical polymer membranous bag of cellular dimensions. This comes as something of an anticlimax to anyone who takes the title of the book too literally.

The honest and exceedingly interesting theme of the book is the potential use of packaged enzymes and detoxicants. The membrane is constructed to allow entry of substrate and the passage out of the product while retaining the enzyme. Toxins would pass through the membrane and become adsorbed onto contained charcoal. Emphasis is laid on the membrane being inert and how enzymes safely kept within this membrane would not be able to elicit an immune cellular response. The approach holds much promise in bio-

medical research and clinical therapy.

There is an enthusiasm pervading the book which makes one overlook a certain amount of repetition. The speculations in chapter 1 would have been better left to the end. The next chapter deals with the procedures for encapsulating microdroplets of cell products, and chapter 3 with the biophysical properties of the different kinds of membranes that can be produced. The experiments described in chapters 4 to 9 are certainly interesting; for example, urease in dialysis bags injected intraperitoneally can act efficiently on endogenous urea, converting it into ammonia; mice with a congenital deficiency in catalase can be furnished with this enzyme; tumours dependent on asparagine could be denied this substance by the presence of asparaginase-loaded dialysis bags. Substitutes for red blood cells bring one up against the importance of not using artificial membranes to which platelets adhere. The use of microcapsules containing charcoal instead of the two-compartment system of the kidney machine to trap waste metabolites seems practical enough, but one is left with the underlying feeling that the safety of the conventional machine is more important than ridding the blood of waste at a faster rate with "artificial cells". But, even so, the general idea of "artificial cells" being used in medical therapy is intriguing and I should imagine that practitioners in this field will welcome this book which draws attention to the state of progress so far made towards what is a difficult target.

B. M. JONES

Whence the Moon

From Plasma to Planet. Edited by A. Elvius. (Proceedings of the Twenty-first Nobel Symposium held in Salysjobaden, Sweden, September 1971.) (John Wiley: New York and London; Almqvist and Wiksell: Stockholm, October 1972.) £10.45.

AT the end of the Apollo manned lunar exploration programme scientists realize that they are on the verge of further exciting discoveries about both the history of the Moon and the origin of the solar system. Many fast-acquired, hard facts about the Moon have been creamed off by investigators using Apollo and Luna data. More subtle facts remain to be prised from the returned samples; and increasingly reliable interpretations will surely derive from continuing studies of lunar rocks and photographs and from the fascinating records now being accumulated via the Apollo experimental stations which continue to function automatically on the Moon's surface.

Lunar elemental abundances point

strongly to the Moon's never having been one part of the Earth: they are indicative, rather, of a Moon which originated from a nebular condensate under rather particular conditions in space. Studies of the ways in which plasmas and gases and particulate clouds behave under the action of an early solar wind are therefore of extreme importance if we are to learn more about the origin of planets—including the Earth itself.

How do atoms and molecules react in interstellar space and in the upper atmosphere of the Earth? What is the respective importance of electric phenomena and gas-dynamical forces in the early solar system? What is the accretion mechanism and the irradiation history of meteoroids? How were asteroids and comets formed? These are some of the fundamental questions raised by the experts who contributed to this volume.

Much may be learned—and cheaply in comparison with the cost of the manned spaceflight programme—by careful, protracted analyses of the smaller objects in the solar system: the dust in the upper atmosphere and in space, the asteroids, and the satellites of other planets. This may be regarded as a realistic view of one of the next steps that scientists may take in their continuing attempts to discover the origin of the planets.

This excellent book, for solar system specialists, physicists, chemists and astronomers, details how these problems are being tackled. At the end of each technical paper, it records valuable discussions between participants at the Nobel Symposium 21. Names such as Alfven, Anders, Arrhenius, Massey, Millman, Petrov and Runcorn feature in the main text and in the discussions; and the book is undoubtedly well worth the price.

G. FIELDER

Homage to Meyerhof

Molecular Bioenergetics and Macromolecular Biochemistry. Edited by H. H. Weber. Pp. viii+197. (Meyerhof Symposium, Heidelberg, July 1970.) (Springer: Berlin and New York, 1972.) 79 DM; \$25.10.

"DISTINCTION develops if nurtured by distinction," wrote Sir Hans Krebs (*Nature*, **215**, 1441; 1967) in tracing the factors that contribute to the making of successful scientists. It is thus perhaps not surprising that, among those who were Otto Meyerhof's former pupils and associates, or whose work was in some way profoundly influenced by him, and who gathered in Heidelberg in July 1970 to commemorate the life and work of that great biochemist, were seven Nobel Laureates as well as many

others who have made major contributions to biochemical knowledge. And it is, perhaps, also not surprising that the lectures given in this symposium are uniformly good: after all, here are the masters, talking about their own achievements. Thus, after a biographical sketch of Meyerhof (by his first pupil, H. H. Weber) and of his ancestry (by H. A. Krebs), there are lucid surveys of the structure and mechanism of action of aldolase (by B. L. Horecker), of the multi-enzyme complexes involved in fatty acid synthesis (by F. Lynen), of chain initiation factors in protein synthesis (by S. Ochoa), and of the amino-acid polymerizations involved in the formation of gramicidin and tyrocidin (by F. Lipmann). There are two fine papers on the structure (by K. C. Holmes) and the activity (by Annemarie Weber) of the actomyosin system of muscle. A fascinating discussion of the genetic basis of carcinogenesis (by L. Sachs) is followed by three equally fine papers on chemical (by M. Eigen) and physiological (by W. Hasselbach and, *in absentia*, by D. Nachmansohn) aspects of membrane processes. As an act of scientific homage to, and of pious remembrance of, a great biochemist and an obviously much-loved person, this symposium cannot be faulted.

One also cannot but applaud the peculiar appropriateness of the occasion. In 1968, the Volkswagen Foundation endowed an Otto Meyerhof Chair at the Weizmann Institute of Science, in Rehovot (Israel), to honour the memory of Meyerhof and to strengthen the relations between Israeli and German scientists. The symposium was planned, at the suggestion of Professor D. Nachmansohn, to commemorate that event, with the participation of German and Israeli scientists: indeed, one of the lecturers, Professor Sachs, is the first holder of the Meyerhof Chair. The symposium was accordingly arranged by a group of the Weizmann Institute, in consultation with Nachmansohn, Ochoa and the Organizing Chairman; it was sponsored by the Institute and the German Gesellschaft für Biologische Chemie. Nothing, surely, could have been more fitting to the occasion and more appropriate to the intention.

But do the proceedings of this symposium make a satisfactory book? With genuine regret, I must conclude that they do not. Such coherence as there is is provided solely by the sentiments of the occasion: as apparent from the contents listed above, there is no cohesive scientific theme. And, alas, there is also little novelty. The substance of much of the material has appeared in print on previous occasions and is now re-reproduced. Indeed, the German text of one excellent lecture is illus-

trated by diagrams, captioned in English, that must surely be familiar to most likely readers of this book and that have obviously been taken directly from another and widely-read publication.

Although this volume will be rightly treasured by those who attended the symposium, as a record of a unique occasion, I cannot imagine that there will be many private purchasers of this very expensive little book.

H. L. KORNBERG

Distribution Theory

Multivariate Analysis. By Anant M. Kshirsagar. Pp. xiv+534 (Marcel Dekker: New York, July 1972.) \$19.50.

THIS book covers the advanced theory of multivariate analysis, concentrating to a large extent on distributional problems. It is a somewhat frightening volume to glance through, as inevitably it has many pages of complicated algebraic expressions; I approached it with some trepidation. It must be confessed, however, that Professor Kshirsagar handles his material so clearly and logically that difficulties are eased. It would be misleading to suggest that they vanish; this is a hard book to read. It is aimed largely at the postgraduate student of mathematical statistics.

It is also misleading to suggest that practical workers seeking guidance in the use of multivariate analysis would find the book helpful. Although the author occasionally presents a brief (and sometimes illuminating) paragraph on practical implications, the text is almost entirely theoretical.

In his presentation, the author makes great use of elegant matrix transformations and random orthogonal transformations, and many of his derivations are relatively neat and concise. Regression analysis plays a key role in the development, and Professor Kshirsagar emphasizes the central part canonical variables and correlations have in multivariate analysis.

Although practical illustrations are not given, there are plenty of references to papers where multivariate analysis has been used. Another feature is a large collection of theoretical exercises which will be valuable to the teacher and student. The appearance of the book is a little off-putting, it apparently having been reproduced directly from a typescript. In view of this, the price seems rather high. There are a number of misprints, and at times the author's style is a little garbled.

To sum up, this is a useful compilation of theoretical results on distribution theory and significance testing in multivariate analysis. It is quite comprehensive, but does not cover factor analysis.

J. F. SCOTT

CORRESPONDENCE

Forestry Policy

SIR,—Your petulant footnotes to Professor Wareing's letter (*Nature*, 241, 414; 1973) are no more convincing than the assertions in your editorial that he so clearly corrected. On forest research there is one further point that needs to be made. The service given to private forestry by the Forestry Commission's research programme, and by individual officers of the Research Division, is of immense value and has been a major factor in the achievement of the very high standard of management now existing in private woodlands. This Society would wish to see the Research Division strengthened rather than dismembered as you suggest.

It is not against the annual operating costs of the state forests that the forest research budget should be assessed, but against the total value of the productive woodlands of Great Britain, a figure in excess of £1,000 million; on such an assessment the modest 0.1% spent on research is surely inadequate.

In your review of *Forestry Policy* in general your unquestioning acceptance of the figures produced by the anonymous team of Government economists, and their theoretical basis, is worrying. Both have been shown to be unsound (*Quart. J. Forestry*, 66, No. 4) and further evidence is accumulating of much available information having been omitted, which, among other things, reverses the costs to the exchequer of jobs in state forestry and in agriculture stated in paragraph 19 of the *Forestry Policy* paper, which you quote. There are other gross errors of assumption, much unrealistic oversimplification, and much defective deduction in the study, which explains why most of it was discarded by ministers in the paper.

You make reference to the agricultural policy of the European Community. I draw your attention first to the Mansholt Plan for Agriculture in the EEC, wherein it is proposed that more than 4 million hectares of agricultural land shall be forested; secondly, to the draft EEC Directive on Forestry signed by the Council of Ministers on January 10, 1973, which details the measures by which this is to be brought about. These measures include: 70 to 90% subsidy for forestation of agricultural land; 50 to 70% subsidy for increasing the productivity of existing woods and forests; an additional annual grant, lasting for 5 to 12 years, for

forestation of marginal agricultural land; cancellation of all subsidies for conversion of woodland to agriculture.

You make no mention of the future needs of this country for timber and wood products. Yet both the rate of consumption, and the cost, continue to rise. In its weak commercial position it is doubtful whether this country can afford the projected level of import, even if the material is physically and politically available, which is also doubtful. Europe is a net importer of wood; the nine EEC countries import 57% of their requirements. In these circumstances the continued expansion of the area of productive forest under sustained management in Great Britain is a prudent and sensible investment.

Your four-point plan for forestry reveals a distressing lack of first hand knowledge. Available literature, much of it free, and the *Guide Map to Your Forests* recently published by Bartholomew for the Forestry Commission which is on sale at booksellers, enable anyone to go and judge for themselves how imaginatively the recreational facilities of the forests are being developed. You will find too that the people who use them do so because of the trees, not in spite of them.

Your vision of the forests being exploited as recreational parks by private commercial organizations is a horrifying one. The attractions and advantages of a silvicultural setting for recreation are many and various; one of the main ones is that the management is in the hands of ecologically trained foresters who love their trees, the land on which they grow, the wealth of wildlife they support, and can interpret their understanding and transmit their enthusiasm to visitors. They are also able to obtain a remarkable degree of local involvement, support, cooperation, and goodwill in developing the cultural potential of their forests, which surely would not be forthcoming under the system you advocate.

Selective planting has been standard silvicultural practice for many years, as has the encouragement of colonization by native species of the land within the forest judged too poor to plant, and of other areas deliberately left unplanted for that purpose.

A 3% return in terms of timber, with the added social benefits of providing rural employment, amenity, shelter, water and wildlife conservation, recreation, sport, the framework of new

landscapes and the perpetuation of existing ones, a primary source of energy, and a form of land use integrated with agriculture, makes forestry one of the best forms of investment for the nation.

Yours faithfully,

P. F. GARTHWAITE

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Good Intentions

SIR,—It gives me no pleasure to criticize well-meaning colleagues for their good intentions regarding suffering mankind ("Vietnam Bombing," *Nature*, 241, 487; 1973), but in politics as in science good intentions alone are not enough.

The notion was advanced that appeals for international morality and the adoption of moral postures by neutralist politicians would do good. What evidence is there to support this hypothesis? During this century two world organizations were established precisely in order to solve the world's many problems in a moral way; let us not shrink from calculating the ratio of successes to failures. Let us also recall with painful nostalgia the politics of the 1930s; then, our kindly, democratic politicians and their well-meaning supporters pursued their moral policies until the political nemesis of 1939; then, distinguished neutralists including Roosevelt and Gandhi—and perhaps also a Scandinavian or two—scored full marks for pontification but zero for knowledge of, and interest in, the relevant power stakes; then, those who bothered to deduce the counterproductivity of such high-minded naivety were abused as warmongers and worse.

If Dr Morten Simonsen is convinced by his historical analyses that preaching is the most effective method for realizing political ends, let him enlighten and convince us—with his examples. But if, like Henry Ford, he dismisses history as bunk, let him not wonder how such men as Talleyrand, Bismarck, Disraeli, Marx, Lenin, and even Kissinger successfully advanced their policies. Can anyone believe that the political wilderness would be more amenable to the moralism of contemporary political babes than it was at the time of the Children's Crusade?

Yours faithfully,

O. LL. LLOYD

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The Burden of Proof

SIR,—The creationists writing in defence of their beliefs are on the wrong tack; no one disputes their right to any theory whatever. What most biologists of my acquaintance abhor are the recent steps three American states have taken to interfere with biology teaching. California, for example, now includes in its guidelines to publishers of school and college texts a statement ("some of the scientific data may be best explained by a creation theory") with which few biologists agree.

The conscientious and informed teacher will ride the blow easily. It is, after all, good teaching if alternative ideas on the origin of species are briefly discussed and rationally dismissed. The teacher should be relating evidence to theory rather than handing out facts. What is unfortunate is that some teachers may be affected by the legislation and will not appreciate the weighting that a specialist in evolution would accord conflicting theories. Modern disciplines depend on the establishment of books, individuals and schools as "authorities". Once such an authority has been set up it is reasonable that conflicting theories gather their evidence and appear as challengers. The workers in the field will then judge the evidence and predictions of the competing ideas. Evolution itself has appeared as a challenger and passed the test while creationism has been demoted; defeated challengers are entitled to retain their views and to search for new evidence but not to pretend to authority. The burden of proof rests with the creationists.

A number of creationists¹⁻³ have written vaguely of "flaws" and "unanswered questions" in evolutionary thought. Such as? Even if there are any, this alone is not enough: creationism must be seen to be a better fit to the data. Only two arguments have been specifically mentioned. One is novel⁴, albeit facetious. This cites some recent attempts⁵ to quantify the role of genetic drift in evolution. Apart from the fact that this role is still contentious itself, evolution by drift is still evolution and not creation. Several creationists try to explain away the fossil record by postulating a succession of creations^{6,7}. This raises a multitude of unanswered questions. How many creations? How often? Why a plurality? Why so many clearly marked trends in fossil series? and so on.

Why do many of *Nature's* correspondents accept the Bible as the ultimate "authority" for the creation theory? This is not only poor biology but poor creationism too, for any archaeologist, theologian or philosopher could tell them that many of the stories in the Bible are

copied from the folk-tales of long-ago tribes more ancient than the Hebrews⁸.

Yours faithfully,

J. P. A. ANGSEESING

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Environmental Education

SIR,—This Institution is now carrying out a survey of current and anticipated provisions at establishments of higher and further education and at schools in the field of education in environmental subjects. A substantial proportion of these establishments have already replied and the information supplied is now being analysed.

May I approach, through the courtesy of your columns, those interested in "environmental education" at various levels to submit private communications of relevance. The aim of this particular exercise is to sample intelligent public opinion outside the official institutions.

Yours faithfully,

J. ROSE

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In Defence of Dingle

SIR,—Well, physics can now rest easy, in the assurance that it has been saved from heresy. Not one, but two occasions have been found in *Nature* to put down Professor Dingle (*Nature*, **239**, 242; 1972; and **241**, 143; 1973). If people really thought that Dingle's work did not deserve serious thought and discussion, would it not have been better to ignore it completely?

When Dingle has failed to get a hearing, and his opponents seem to agree on little except the fact that they are opponents, it would be of little use for me to say anything on the matter as a piece of physics. But there are two or three general comments, which anyone might make, and which someone should make.

In the first place, Dingle was once recognized to be an authority in this matter. If he has now come to different conclusions, either there are good

reasons for these second thoughts, or else they are to be put down as a foible of old age. But the writing is certainly not that of a senile man.

In the second place, it would appear that none of his critics has faced Dingle's points that (a) he was discussing physics, not mathematics; and (b) that all of the alleged experimental verifications involve circular arguments in their interpretation.

In the third place, if it should turn out that there is some truth in Dingle's views, the way in which they seem to have been brushed aside will not be likely to make science stand any higher in the public esteem. In the United States, especially, the "Velikovsky affair" left a bad taste in many mouths; it is surely not wise to seem to persecute another man, and one whose views are by no means so unorthodox.

Yours faithfully,

H. L. ARMSTRONG

Addendum

In the article "The First Fossil Record of Caecilian Amphibians" by R. Estes and M. H. Wake (*Nature*, **239**, 228; 1972) the identification for Fig. 1 *k-o* was omitted from the figure legend. It should read: *k-o*, *Geotrypetes seraphinii*, MVZ 98253.

Announcements

International Meetings

March 22, **13th International Technical Scientific Meeting on Space** (Secretariat, Via Crescenzo n.9, 00193 Roma).

March 26–30, **Annual Chemical Congress** (Dr J. F. Gibson, The Chemical Society, Burlington House, London W1).

March 27–29, **Ultrasonic Conference and Exhibition** (Ultrasonic International '73, IPC Science and Technology Press Ltd, IPC House, 32 High Street, Guildford, Surrey).

March 27–29, **PowTech International Powder Technology and Bulk Solids Exhibition and Conference** (Specialist Exhibitions Ltd, Green Dragon House, 64 High Street, Croydon, Surrey).

March 27–29, **The Practical Implications of Fracture Mechanisms** (Meetings Secretary, The Institution of Metallurgists, Northway House, London N20).

March 28, **Corrosion and Deterioration of Metals and Alternative Engineering Materials** (Assistant Secretary, 14 Belgrave Square, London SW1).

March 28–30, **Nuclear Structure and High Energy Physics**. (The Meetings Officer, The Institute of Physics, 47 Belgrave Square, London SW1).

March 29, **Rancidity in Fatty Foods** (Mr J. Watson-Walker, Symposium Secretary, Department of Chemistry, The University of Technology, Loughborough, Leicester).

March 29–31, **Tenth Symposium on Biomathematics and Computer Science in the Life Sciences** (Office of the Dean, The University of Texas Graduate School of Biomedical Sciences, Division of Continuing Education, PO Box 20367, Houston, Texas 77025).

March 29–31, **Archaeometry and Archaeological Prospection** (Mrs Romie Iplady, Research Laboratory for Archaeology and the History of Art, 6 Keble Road, Oxford).

April 2–3, **Society for Electrochemistry, Spring Informal Discussion Meeting** (Dr J. E. B. Randles, Department of Chemistry, Haworth Building, The University of Birmingham, PO Box 363, Birmingham B15 2TT).

April 3–6, **Tenth International Mineral Processing Congress** (Imperial College, Exhibition Road, South Kensington, London SW7).

April 3–6, **Activated Carbon in Water Treatment** (The Water Research Association, Medmenham, Marlow, Buckinghamshire SL7 2HD).

April 3–13, **Education of Teachers for Integrated Science** (Science Teaching Center, University of Maryland, College Park, Maryland 20742 USA).

April 4, **New Techniques and Applications in Scanning Electron Microscopy** (Meetings Officer, The Institute of Physics, 47 Belgrave Square, London SW1X 8QX).

April 9–11, **Oligosaccharides** (Dr W. R. Williams, Chemistry Department, Birkbeck College, Malet Street, London WC1E 7HX).

April 9–11, **Seventh Thin Films Conference** (Meetings Officer, The Institute of Physics, 47 Belgrave Square, London SW1X 8QX).

April 9–12, **Cancer Detection and Prevention** (Secretary, Istituto Di Oncologia "F. Addari", Viale Ercolani 4/2 40138 Bologna, Italy).

April 10–13, **Fifth National Atomic and Molecular Physics Conference** (Institute of Physics, 47 Belgrave Square, London SW1X 8QX).

April 10–13, **Propagation of Radio Waves at Frequencies above 10 GHz** (Institute of Electrical and Electronics Engineers).

April 13, **Symposium on the Monitoring of Electron Capture Nuclides and Soft Beta Emitters** (J. R. A. Lakey, Publicity Secretary, British Radiological Protection Association, c/o Royal Naval College, Greenwich, London SE10).

April 15–19, **The "Sea Peoples"** (Professor R. A. Crossland, Department of Greek, The University, Sheffield S10 2TN).

April 15–19, **Industrial Aspects of Biochemistry** (The Secretariat, FEBS Special Meeting, IMA Conference Centre, 10 Fitzwilliam Place, Dublin 2, Ireland).

April 15–20, **57th Annual Meeting of the Federation of American Societies for Experimental Biology** (Mrs T. C. Heatwole, Director, 5110 West Franklin Street, Richmond, Virginia 23226).

April 16, **Current Progress in Palaeobotany in Britain** (Dr Keith Allen, Department of Botany, The University, Bristol BS8 1UG).

April 16–18, **Liquid State** (Professor J. G. Powles, The Physics Laboratories, The University, Canterbury, Kent. Details also from Meetings Officer, The Institute of Physics, 47 Belgrave Square, London SW1X 8QX).

April 29–May 5, **Euchem Conference on Stereochemistry** (Professor R. H. Martin, Department de Chimie Organique, Université Libre de Bruxelles, 50, Ave. F.-D. Roosevelt 1050 Bruxelles/Belgique).

April 30–May 1, **Electro-Optics Principles and Applications** (National Offices, PO Box 288, Redondo Beach, California 90277).

Reports and Publications

not included in the Monthly Books Supplement

Great Britain and Ireland

Coal and Energy Policy in Europe: a Report by the British Coal Industry. (Report issued jointly by the National Coal Board; British Association of Colliery Management; National Association of Colliery Overmen, Deputies and Shotfriers; National Union of Mineworkers; Institution of Mining Engineers.) Pp. 9. (London: National Coal Board, 1972.) [1812]

Royal Observatory Annals. No. 7: Photometric Standard Stars. By A. W. J. Cousins. Pp. 86. (Herstmonceux: Royal Greenwich Observatory, 1972.) £1.15 net. [1812]

The International Commission on Radiological Protection. ICRP Publication 19: The Metabolism of Compounds of Plutonium and other Actinides. (A Report prepared by a Task Group of Committee 2 of the ICRP.) Pp. 59. (Oxford and New York: Pergamon Press, 1972. Published for the ICRP.) £1.50. [1812]

Bulletin of the British Museum (Natural History). Zoology. Vol. 23, No. 3: The Gunung Benom Expedition 1967. 4. New Records of Malayan Bats, with Taxonomic Notes and the Description of a New *Pipistrellus*. By J. E. Hill. Pp. 21–42. 85p. Vol. 23, No. 9: The Gunung Benom Expedition 1967. 11. Notes on Zoogeography, Convergent Evolution and Taxonomy of Fleas (Siphonaptera), Based on Collections from Gunung Benom and Elsewhere in South-East Asia. 1. New Taxa (Pygiopsyllidae, Pygiopsyllinae). By R. Traub. Pp. 201–305+58 plates. £7.15. (London: British Museum (Natural History), 1972.) [1812]

Geological Survey of Ireland. Special Paper No. 2: Upper Old Red Sandstone and Lower Carboniferous of the Slieve Beagh Syncline and Its Setting in the Northwest Carboniferous Basin, Ireland. By D. Sheridan. Pp. vi+129+plates 10–21. (Dublin: Geological Survey Office, 1972.) [1812]

Toxicological and Environmental Chemistry Reviews. Vol. 1, Numbers 1/2, June 1972. Edited by Roland W. Frei and Otto Hutzinger. Subscription Rates (per volume postpaid). 4 issues per volume. Great Britain: Libraries £17.25; individuals who warrant the journal is for their own use and order direct from the publisher, £5.15. USA/elsewhere: Libraries \$45/£18.75. Individuals who warrant the journal is for their own use and order direct from the publisher, \$16/£6.65. (London and New York: Gordon and Breach, Science Publishers, 1972.) [1812]

Department of the Environment; Scottish Office. Committee on the Rating of Plant and Machinery—Report. Pp. iv+26. (London: HMSO, 1972.) 26p net. [1812]

Biochemical Education, Vol. 1, No. 1, Autumn 1972. (A Quarterly Bulletin of the International Union of Biochemistry.) Pp. 1–16. Subscription: £2; \$6 for 4 issues. (Leeds: Biochemical Education, Department of Biochemistry, 9 Hyde Terrace, 1972.) [1912]

The University of Hull. Annual Report of the Council and the Senate to the University Court, 1971/1972. Pp. 179. (Hull: The University, 1972.) [2012]

The Orthopaedically Handicapped Child: Social, Emotional and Educational Adjustment—An Annotated Bibliography. By Doria Pilling. Pp. 56. (Windsor: National Foundation for Educational Research, Book Division, 2 Jennings Buildings, Thames Avenue, 1972.) £1.20. [2012]

Greater London Council Scientific Branch. Annual Report of the Scientific Adviser 1971. Pp. 115. (London: Greater London Council, 1972.) £2. [2112]

Department of the Environment. The Welsh Office. Report of a River Pollution Survey of England and Wales. Volume 2: Discharges and Forecasts of Improvement. Pp. xiii+231. (London: HMSO, 1972.) £4.60 net. [2112]

Department of Education and Science. Sources of Information on European Organisations. Pp. v+22. (London: Department of Education and Science, 1972.) [2112]

Bulletin of the British Museum (Natural History). Entomology. Vol. 27, No. 7: Contributions Towards a Revision of *Myrsidea* Waterston. VII. (Phthiraptera: Amblycera: Menoponidae.) By B. K. Tandan. Pp. 369–410+2 plates. (London: British Museum (Natural History), 1972.) £1.95. [2112]

Some Aspects of Process Licensing in the Fertiliser Industry. By J. D. C. Hemsley. Pp. 15. (London: The Fertiliser Society, 1972.) [2112]

Ministry of Posts and Telecommunications. Report of the Television Advisory Committee. Pp. 21. (London: HMSO, 1972.) 14½p net. [2112]

Nuclear Enterprises. 1972 Scintillator Catalogue. Pp. 28. (Edinburgh: Nuclear Enterprises, Ltd. Sighthill, 1972.) [2712]

Laboratory Report on Biological Transmutation. By Dr D. B. Long. Pp. 20. (Braintree, Essex: Henry Doubleday Research Association, 20 Convent Lane, Bocking, 1972.) 20p. [2812]

The Royal Society. Scientific Research in Schools Committee—Report to Council 1972. Pp. 20. (London: The Royal Society, 1972.) [2812]

Centre for Environmental Studies. Fifth Annual Report, April 1971 to March 1972. Pp. 57. (London: Centre for Environmental Studies, 1972.) [2912]

Kent Instruments and the Metallurgical Industry. Pp. 22. (Luton, Bedfordshire: Kent Instruments Limited, 1972.) [2912]

Hydrogen Thyrratrons—Preamble. Pp. 50. Storage Tubes—Preamble. Pp. 24. (Chelmsford, Essex: English Electric Valve Co., Ltd., 1972.) Gratis. [11]

Forestry Commission. Fifty-second Annual Report and Accounts, 1971–72. Pp. 102 (8 plates). 75p. Report on Forest Research 1972. Pp. vii+193+10 plates. £1.60 net. Forest Record No. 84: Winter Temperatures and Survival of the Green Spruce Aphid. By C. I. Carter. Pp. 10. 7p. (London: HMSO, 1972.) [21]

Department of the Environment. Welsh Office. Rate Rebates in England and Wales, 1971–72. Pp. 65. (London: HMSO, 1972.) 82p net. [31]

British Medical Bulletin. Vol. 29, No. 1, January 1973: Symposium on Biological Basis of Radiotherapy. Pp. 1–90. (London: The British Council, 1973.) UK £2.25; other countries £2.50. [31]

Understanding the City of the Future. By A. G. Wilson. (Reprinted from *The University of Leeds Review*, Vol. 15, No. 1.) Pp. 32. (Leeds: The University, 1972.) [41]

The Scientific Proceedings of the Royal Dublin Society. Series A. Vol. 4, No. 16: Acromyces of Oak Park, Co. Carlow, Ireland. By Q. D. MacGarvie. Pp. 219–230. 40p. Vol. 4, No. 17: The Silurian of the Crough Patrick Range, Co. Mayo. By M. J. Bickle. R. G. W. Kidd and Euan Nisbet. Pp. 231–250+plate 10. 75p. Vol. 4, No. 18: Award of the Boyle Medal to John Lighton Syngé, F.R.S. Pp. 251–252. 10p. Vol. 4, No. 19: Geometry and Physics. By J. L. Syngé. (Boyle Medal Lecture.) Pp. 253–274. 75p. Vol. 4, No. 20: Artificial Key for the Identification of the Inflorescence Phase of Irish Grasses. By M. A. Farragher. Pp. 275–294+plates 11 and 12. £1. Vol. 4, No. 21: Poaceae—Irish Members. Part 2: Artificial Key for the Identification of the Vegetative Phase of Irish Grasses. By M. A. Farragher. Pp. 295–304+plate 13. £1. Series B. Vol. 3, No. 9: Counts of Infective Units of the Take-All Fungus in Co. Donegal Oat Soils. By M. J. Downes. Pp. 119–126. 35p. (Dublin: Royal Dublin Society, 1972.) [41]

Geological Excursion Guide to the Assynt District of Sutherland. By M. MacGregor and J. Hemmister. Third edition, with an Appendix by M. R. W. Johnson. Pp. 68. (Edinburgh: Edinburgh Geological Society, 1972.) 60p. [51]

Bulletin of the British Museum (Natural History). Geology. Vol. 22, No. 2: Llandovery Conodonts from the Welsh Borderland. By R. J. Aldridge. Pp. 125–231+9 plates. (London: British Museum (Natural History), 1972.) £4.45. [51]

Ion Exchange and Membranes: Science and Technology of Dynamic Macromolecules. Vol. 1, No. 1, August 1972. Edited by J. A. Mikes. Pp. 1–72. Subscription rates (per volume post paid), 4 issues per volume: Libraries and Institutions, USA/elsewhere \$45; £18.75; Great Britain £17.25. Individuals (who warrant the journal is for their own use and order direct from the publishers), USA/elsewhere \$16; £6.65; Great Britain £5.15. (London and New York: Gordon and Breach Science Publishers, 1972.) [51]

Other Countries

Fisheries Research Board of Canada. Technical Report No. 329: Investigations into the Effects on Lobsters of Raking Irish Moss, 1970-1971. By D. J. Scarraut. Pp. 34. (St. Andrews, NB: Fisheries Research Board of Canada, Biological Station, 1972.) [1912]

Canada: Department of Energy, Mines and Resources. Paper 71-14: Upper Paleozoic Stratigraphy of the Eagle Plain Basin, Yukon Territory. By H. L. Martin. Pp. iii+54. \$2. Paper 72-33: Rubidium-Strontium Isochron Age Studies, Report 1. By R. K. Wanless and W. D. Loveridge. Pp. vii+77. \$2. Paper 72-27: Fluvial Sedimentary Structures Formed Experimentally in a Pipe, and Their Implications for Interpretation of Subglacial Sedimentary Environments. By B. C. McDonald and J. S. Vincent. Pp. vi+30. \$2. Paper 71-45: Geology of Malpeque-Summerside Area, Prince Edward Island. By V. K. Prest. Pp. vi+21. \$2. Paper 72-3: 1971-1972 Index of Publications of the Geological Survey of Canada. Pp. 65. \$1.50. Geological Map 1300A: Eureka Sound South, District of Franklin. (Ottawa: Information Canada, 1972.) [1912]

The Walter and Eliza Hall Institute of Medical Research 1971/1972. Pp. 137. (Melbourne: The Walter and Eliza Hall Institute of Medical Research, Royal Melbourne Hospital, 1972.) [1912]

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Journal of Structural Mechanics, Vol. 1, No. 1, 1972. Edited by E. F. Masur, in association with Antoni Sawczuk. Pp. 1-158. Published four times annually. Subscription rate for Vol. 1 (1972) containing 4 issues is \$55. Postage outside the US and Canada is \$3 per volume. (New York: Marcel Dekker, Inc., 1972.) [1912]

Australia: Commonwealth Scientific and Industrial Research Organization. Annual Report of the Division of Irrigation Research, 1971/1972. Pp. iv+72. (Griffith, NSW: CSIRO, 1972.) [1912]

Communications in Statistics, Vol. 1, No. 1, 1973. Pp. 1-92. Published six times a year. Subscription for Volume 1 (1973) containing 6 issues is \$35. Charge per volume for postage outside the US and Canada is \$3.60. Special discount rate for individual professionals and students is \$15. (New York: Marcel Dekker, Inc., 1972.) [1912]

Separation and Purification Methods, Vol. 1, No. 1, 1972. Edited by Edmond S. Perry and Carol J. van Oss. Pp. 1-236. Subscription rate: \$19.50 per volume, 2 issues. Charge per volume for postage outside the US and Canada \$1.50. (New York: Marcel Dekker, Inc., 1972.) [1912]

Comité International des Poids et Mesures. Comité Consultatif de Photométrie, 7e Session, 1971 (1-2 septembre). Pp. 135. (Sèvres, France: Bureau International des Poids et Mesures, 1972.) [2012]

Gouvernement du Québec. Le Conseil des Recherches Agricoles. Recherches Agronomiques—Sommaire des Résultats 1970/1971. (No. 16.) Pp. 151. (Québec: Ministère de l'Agriculture et de la Colonisation, 1972.) [2012]

Annual Report of the Mauritius Institute for 1971. Pp. 15. (Port Louis: Government Printer, 1972.) Rs.2. [2012]

Western State of Nigeria. Annual Report on the Forest Administration of Western Nigeria, 1966-67. Pp. i+35. (Lagos: Ministry of Agriculture and Natural Resources, 1971.) 3s. 6d. [2012]

United States Department of the Interior: Geological Survey. Professional Paper 707: Interpretation of an Aeromagnetic Survey of the Amchitka Island Area, Alaska. By G. D. Bath, W. J. Carr, L. M. Gard, Jr., and W. D. Quinlivan. Pp. iv+25. (Washington, DC: Government Printing Office, 1972.) [2112]

Smithsonian Contributions to Zoology. No. 129: Two New Species and a New Subgenus of Lucinidae (Mollusca: Bivalvia), with Notes on Certain Aspects of Lucinid Phylogeny. By Joseph C. Britton, Jr. Pp. 19. 35 cents. No. 131: Two New Caridean Shrimps, One Representing a New Family, from Marine Pools on Ascension Island (Crustacea: Decapoda: Natantia). By Fenner A. Chace, Jr., and Raymond B. Manning. Pp. 18. 30 cents. (Washington, DC: Smithsonian Institution Press, 1972. For sale by US Government Printing Office.) [2112]

United States Department of the Interior: Geological Survey. Water-Supply Paper 2135: Surface Water Supply of the United States 1966-70. Part 14: Pacific Slope Basins in Oregon and Lower Columbia River Basin. Prepared in co-operation with the States of Oregon and Washington and with other agencies. Pp. x+1036. (Washington, DC: Government Printing Office, 1972.) \$4.25. [2712]

Carnegie Institution. Annual Report of the Director of the Department of Terrestrial Magnetism, 1971-1972. (Reprinted from *Carnegie Institution Yearbook* 71, for the year July 1, 1971-June 30, 1972.) Pp. 215-341. (Washington, DC: Carnegie Institution, 1972.) [2712]

Institutt for Atomenergi, Kjeller, Norway. Kjeller Report No. 147: Ramona II—a Fortran Code for Transient Analysis of Boiling Water Reactors. By R. Holt and J. Rasmussen. Pp. iv+120+appendix. (Kjeller, Norway: Institutt for Atomenergi, Kjeller Research Establishment, 1972.) [2812]

US Department of the Interior: Geological Survey. Bulletin 1345: Precambrian Rocks in the Cordes Area, Yavapai County, Arizona. By C. A. Anderson. Pp. iv+36+2 plates. (Washington, DC: Government Printing Office, 1972.) [2912]

Annals of the Transvaal Museum, Vol. 28, No. 5: Revision of the Genus *Brownacris* Dirsh, 1958, with Descriptions of New Species (Orthoptera: Acridoidea). By H. Dick Brown. Pp. 47-78. (Pretoria: Transvaal Museum, 1972.) [2912]

Smithsonian Contributions to Zoology. No. 130: Synopsis of the Tribe Omobranchini with Descriptions of Three New Genera and Two New Species (Pisces: Blenniidae). By Victor G. Springer. Pp. 31. (Washington, DC: Smithsonian Institution Press, 1972. For sale by US Government Printing Office.) 50 cents. [2912]

Annals of the South African Museum. Vol. 60, Part 1: The Origin, Interrelationships and Distribution of Southern African Rajidae (Chondrichthyes, Batoidae). By P. A. Hulley. Pp. 1-103. R.7.50. Vol. 60, Part 2: Redescription of *Pandaka silvana* (Barnard), (Pisces: Gobiidae). By M. J. Penrith and Mary-Louise Penrith. Pp. 105-108. R.1. Vol. 60, Part 3: Pliocene Marine Invertebrates from Langebaanweg, Cape Province. By Brian Kensley. Pp. 173-190. R.2. Vol. 60, Part 5: The Rare Plectognath Fish, *Marcorhamphosodes uradoi*, in South African Waters. By P. A. Hulley. Pp. 191-195. R.1.20. Vol. 60, Part 6: A Report on the Mesopelagic Fishes Collected During the Deep-Sea Cruises of R.S. *Africana II*, 1961-1966. By P. A. Hulley. Pp. 197-236. R.3.50. Vol. 60, Part 7: Mesopelagic Fishes from Vema Seamount (IK Station 52). By P. A. Hulley. Pp. 237-244. R.1.70. Vol. 60, Part 8: The Cretaceous Stratigraphy of San Nicolau and Salinas, Angola. By Michael R. Cooper. Pp. 245-251. R.1.85. Vol. 60, Part 9: A New Species of Southern African Brevitajid Skate (Chon-

drichthyes, Batoidae Rajidae). By P. A. Hulley. Pp. 253-263. (Cape Town: South African Museum, 1972.) [2912]

Canada: Department of Energy, Mines and Resources. Geological Survey of Canada. Paper 71-48: Reconnaissance Geology of a Part of the Precambrian Shield, Northeastern Quebec and Northern Labrador, Part 3. By F. C. Taylor. Pp. v+14. \$1.50. Paper 72-14: Surficial Geology of Tasko Lakes Map-Area, British Columbia. By J. A. Heginbottom. Pp. v+9. \$2. Paper 72-30: "Standard Samples" of Silicate Rocks and Minerals—a Review and Compilation. By Sydney Abbey. Pp. v+13. \$1.50. (Ottawa: Information Canada, 1972.) [11]

World Health Organization. Technical Report Series, No. 511: Development of Environmental Health Criteria for Urban Planning—Report of a WHO Scientific Group. Pp. 35. (Geneva: WHO; London: HMSO, 1972.) 4 Sw. francs; 40p; \$1. [11]

US Department of the Interior: Geological Survey. Bulletin 1352: Selected Annotated Bibliography on Asphalt-Bearing Rocks of the United States and Canada to 1970. By Marjorie C. Mullens and Albert E. Roberts. Pp. iv+218. (Washington, DC: Government Printing Office, 1972.) \$1.25. [11]

Australia: Commonwealth Scientific and Industrial Research Organization. Annual Report of the Marine Biochemistry Unit. Compiled by M. P. Titterton. Pp. 15. (Sydney: CSIRO, 1972.) [11]

Fisheries Research Board of Canada. Technical Report No. 349: Recaptures and Movements of Tagged Snow Crabs (*Chionoecetes opilio*) for the Gulf of St. Lawrence. By J. Watson and P. G. Wells. Pp. 12. (St. Andrews, NB: Fisheries Research Board of Canada, Biological Station, 1972.) [11]

Transactions of the American Philosophical Society. New Series—Vol. 62, Part 7: Burmese Earthworms—an Introduction to the Systematics and Biology of Megadrile Oligochaetes with Special Reference to Southeast Asia. By G. E. Gates. Pp. 326. (Philadelphia: The American Philosophical Society, 1972.) \$12. [11]

Australia: Repatriation Department. Medical Research Bulletin No. 5: Blood Pressure—Age Relationships of Australian Ex-Servicemen Classified in 87 Disease Categories. By R. V. Southcott, L. G. Veitch and R. B. Cunningham. Pp. 17. (Adelaide: Repatriation Department, 1972.) [11]

Queensland. Twenty-seventh Annual Report of the Council of the Queensland Institute of Medical Research for the year ended June 30, 1972. Pp. 25. (Brisbane: Government Printer, 1972.) [21]

Smithsonian Contributions to Paleobiology. No. 12: The *Bradleya* Problem, with Descriptions of Two New Psychrospheric Ostracode Genera, *Agrenocythere* and *Poseidonamicus* (Ostracoda: Crustacea). By Richard H. Benson. Pp. iv+138. (Washington, DC: Smithsonian Institution Press, 1972. For sale by US Government Printing Office.) \$2.50. [31]

US Department of the Interior: Geological Survey. Bulletin 1331-B: The Canaan Peak, Pine Hollow, and Wasatch Formations in the Table Cliff Region, Garfield County, Utah. By William E. Bowers. Pp. iii+39+plate 1. (Washington, DC: Government Printing Office, 1972.) 70 cents. [31]

Republic of Cyprus. Ministry of Agriculture and Natural Resources. Geological Survey Department Bulletin No. 6: The Geology of the Bellapais-Kytherea Area of the Central Kyrenia Range. By Charles Ducloz. Pp. 75. (Nicosia: Geological Survey Department, 1972.) [31]

Suomen Geodeettisen Laitoksen Julkaisuja/Publications of the Finnish Geodetic Institute. No. 73: Reduction of Astronomical Latitudes and Longitudes 1922-1948 into the FK4 and CIO Systems. By V. R. Olander. Pp. 44. No. 74: Photoelectric Time Micro-meter. By J. Kakkuri and K. Kalliomäki. Pp. 58. (Helsinki: Finnish Geodetic Institute, 1972.) [51]

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